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The Effect of OsteoEze Gold™ on the Inflammatory Marker CRP and Quality of Life in Osteoarthritis of the Knee

A research dissertation submitted to the Faculty of Health Sciences, University of Johannesburg, as a partial fulfilment for a Masters degree in technology: Homoeopathy by

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DECLARATION

I, Romy C. Levy, do hereby declare that this is my own unaided work, except where otherwise indicated in the text. This research dissertation is being submitted for the degree of Master’s in Technology: Homoeopathy at the University of Johannesburg. It has not been previously submitted for any degree or examination at any other Technikon or University.

_____________________________________                                     ___________________

Romy C. Levy                                                                                        Date
ABSTRACT

Osteoarthritis (OA) is a chronic and debilitating condition, characterized by irreversible damage to the joint space, most commonly affecting the knees, hips, hands and spine (Colledge et al., 2010). OA is the leading cause of joint pain and disability in middle-aged and elderly persons (Long et al., 2001). The prevalence of OA of the knee in adults living in the United States has grown from a reported 21 million in 1990 to a total estimate of 26.9 million in 2005 (CDC, 2011). By the age of 65 years, 80% of the total population has been reported as showing radiographic evidence of OA; while a 20-30% of the total population is symptomatic with radiographic evidence of OA (Doherty et al., 2006).

Conventional treatment for OA of the knee is aimed at pain management by use of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs). Some negative effects of these drugs include drug dependency, liver and kidney damage, cardiovascular pathologies, gastric upset and depression. Corticosteroid injections are also used to alleviate chronic inflammation and joint pain, but may lead to further joint destruction (Shamoon and Hochberg, 2000; Mayo Foundation for Medical Education and Research, 2011).

OsteoEze Gold™ is a nutraceutical product that contains chondroitin sulphate, glucosamine sulphate, vitamin C and manganese. In combination, the constituents of OsteoEze Gold™ have been shown to be useful in the treatment for OA of the knee (Clegg et al., 2006). In addition, studies have shown that these ingredients prove effective in reducing moderate to severe pain in sufferers of OA of the knee (Vidyasagar et al., 2004).

The aim of this study was to determine the effect of OsteoEze Gold™ on the inflammatory marker C-reactive protein (CRP) and quality of life in OA of the knee using blood tests and the Arthritic Impact Measurement Scales (AIMS2SF) respectively.

This was a 16-week, double blind, placebo-controlled study using matched pairs according to age, gender and severity of symptoms, and formed part of a group study, with another researcher, who utilized the Intermittent and Constant Osteoarthritis Pain scale (ICOAP) Short Physical Performance Battery (SPPB) and the same sample.

Seventy-seven participants, from a target group of males and females, between the ages of 40 and 70 years, were recruited from print advertisements and by word-of-mouth (Appendix A) at
the University of Johannesburg, Doornfontein campus (DFC). Forty-eight participants (21 in the control group; 27 in the treatment group) from the sample completed the study.

At the initial consultation (week 0) and the second consultation (week 8) participants in the experimental group received an 8-week supply of OsteoEze Gold™ capsules (two bottles containing 126 capsules each) while the control group received placebo capsules (two bottles containing 126 capsules). Participants were requested not to take any other medication or supplements for the treatment of OA of the knee for the duration of the study, with the exception of paracetamol for pain relief, which was to be recorded on the medication record form (Appendix D).

The effects of OsteoEze Gold™ in the treatment of OA of the knee was tested by using the AIMS-SFV2 (Appendix E) to assess quality of life, while C-reactive protein (CRP) was used to assess levels of inflammation. The AIMS-SFV2 and CRP were conducted at the initial consultation, the 8-week consultation and final 16-week consultation. The results were statistically analysed to assess the participant’s progress (Meenan et al., 2004).

The results for the AIMS-SFV2 showed no statistically significant relevance in the placebo group, over the full duration of the study. In the treatment group however there was statistically significant relevance seen in sections E, F and J of the AIMS-SFV2. There were statistically significant differences seen in the inter-group analysis of section F at week 8. Additionally, there was a statistically significant change seen in the intra-group analysis in section E for the treatment group only and section J for both groups. There was statistically significant change that occurred in section J, referring to over-all wellness, and section E, referring to the participants’ social activities, occurred between the initial consultation (0 weeks) and the final consultation (16 weeks), concluding that there was an increase state of mental and emotional well-being those participants in the treatment group.

There was no statistically significant difference in the values for CRP over the course of the 16-week trial in either the placebo group or the treatment group (p >0.05) (Becker, 2013). This may be attributed to the well-established correlation between obesity, cardiovascular disease (CVD) and OA of the knee, and the resultant elevation of blood plasma CRP.

Supplementation with OsteoEze Gold™ may thus improve the suffering of OA the knee without directly reducing the elevated levels of blood plasma CRP (Matsumo et al., 2008).
This dissertation is lovingly dedicated to my husband, Avin B. Levy and my two children, Liora Hadassah and David Zaev Levy. The love and support you have given to me through this process has meant more than words can express. The sacrifices each of you have made over the past few years has given me the opportunity to grow mentally, emotionally, spiritually, physically and financially and thus given us the strength as a family to weather any storm. I love you all so very much and look forward to our future filled with Hashems richest brochas.
AKNOWLEDGEMENTS

I would like to extend my most heartfelt thanks and acknowledgment to those of you who granted me support, encouragement, and love through this seven-year journey. You are an inspiration to me in so many ways, and I am so immensely grateful for each and every one of you in my life:

- My mom, Leonor Schneider, for your unending love. You always told me that I would be able to accomplish anything in my life. Mom, thank you, I love you now and always. You are a constant source of inspiration to be able to overcome any and all adversity. You always come out smiling and inspire me to do the same.
- My sister Amy Meyerowitz, my best friend and confidant. You have always made me laugh in the sad times, smile bigger in the happy times and are a shoulder for me to rely on for anything. You have always affirmed me: I am so blessed to have you in my life, thank you for always believing in my abilities.
- My cousin, Mark Dermick, who has always loved me and given to me like a father to a daughter. You set me on a spiritual path of self-actualization and therefore helped give me the opportunity to be the person who I am today. Thank you so much for all that you have given to me. I love you, bokkie.
- Gogo Edith Chinungu and Gogo Alice Milo
- Mrs. Helen Heldemuth
- Mr. Colin and Mrs. Gillian Gamsu
- My aunty Carmela and uncle Basil Lishansky
- The Cahn family, the Sussman family, the Brom family
- Mr. Colin Kapaluschnik
- Dr. Chanel Martin, Mrs. Andrea Levy and the Killarney Riviera Pharmacy Team
- Dr. Marelize Caminsky, Dr. Yolande Olivier, Dr. Graham Yutar, Dr. Neil Gower
- Mrs. Anne Aitken, Mr. Denis Moadhin and the SoPure Laboratories Team
- Nativa (Pty) Limited for generously funding this study
- National Health Laboratory Services for conducting the pathology testing
- Jurgins Becker for analysing the statistical data
- Pierre and Lynn and the Post Net Killarney Team
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CHAPTER ONE

INTRODUCTION

1.1 Problem Statement

Osteoarthritis (OA) is defined as a chronic and debilitating condition, characterized by irreversible damage to the joint space, most commonly affecting the knees, hips, hands and spine (Colledge et al., 2010). OA is the leading cause of joint pain and disability in middle-aged and elderly persons (Long et al., 2001). The prevalence of OA of the knee in adults living in the United States has grown from a reported 21 million in 1990 to a total estimate of 26.9 million in 2005 (CDC, 2011). After the age of 50 years, OA is seen to be more commonly found in women than in men, postulated as being resultant of a postmenopausal decline in oestrogen (Dickson and Hosie, 2003). By the age of 65, 80% of the total population have been reported as showing radiographic evidence of OA; 20-30% of the total population are symptomatic with radiographic evidence of OA (Doherty et al., 2006).

Conventional treatment for OA of the knee includes, pain management by use of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs). Some negative effects of these drugs include drug dependency, liver and kidney damage, cardiovascular pathologies, gastric upset and depression. Corticosteroid injections are also used to alleviate chronic inflammation and joint pain but may lead to further joint destruction (Shamoon and Hochberg, 2000; Mayo Foundation for Medical Education and Research, 2011). OsteoEze Gold™ is a nutraceutical product that contains chondroitin sulphate, glucosamine sulphate, vitamin C and manganese. In combination, the constituents of OsteoEze Gold™ have been shown to be useful in the treatment for OA of the knee (Clegg et al., 2006). In addition, studies have shown that these individual ingredients prove effective in reducing moderate to severe pain in sufferers of OA of the knee (Vidyasagar et al., 2004).

1.2 Aim of the Study

The aim of this study was to determine the effect of OsteoEze Gold™ on the inflammatory marker C-reactive protein (CRP) and quality of life in OA of the knee using blood tests and the Arthritic Impact Measurement Scales (AIMS2SF) respectively.
1.3 Benefits of the Study

An anticipated positive result of this research may provide evidence that a formulation of chondroitin sulphate, glucosamine sulphate, vitamin C and manganese may reduce problematic levels of the inflammatory marker CRP and improve the overall quality of life of people suffering with OA of the knee. This may form a basis for larger scale and more lengthy investigations into the use of OsteoEze Gold™ in treating OA of the knee.

1.4 Hypothesis

The proposed hypothesis is that OsteoEze™ Gold will improve the quality of life and reduce the plasma levels of CRP in the treatment group compared to those participants in the placebo group. Therefore OsteoEze Gold™ will prove to be effective in decreasing the symptoms of pain and debility experienced by the participants in the treatment group; while there will be no significant changes in those participants receiving the placebo capsule.

1.5 Null Hypothesis

The null hypothesis is that OsteoEze™ will not provide a significant improvement in the quality of life and a reduction in the levels of plasma CRP in those patients suffering with OA of the knee over a period of 16 weeks, in the treatment group compared to those taking the placebo capsules.
CHAPTER TWO

LITERATURE REVIEW

2.1 Osteoarthritis of the Knee

2.1.1 Definition

Osteoarthritis (OA) of the knee is a degenerative joint disease characterized by clinical and biochemical changes that account for the signs and symptoms of the condition, such as joint pain, impairment of mobility of the affected joints, and eventually disability (Shiel and Stoppler, 2008; Colledge et al., 2010). OA may be best described as an active disease process, leading to destruction of articular joint cartilage and resultant pathological osteological formations (Peat et al., 2001). It is a chronic, debilitating condition characterized by irreversible damage of the joint space and its supporting cartilage. OA most commonly affects the knees, hips, hands and spine (Colledge et al., 2010).

2.1.2 Prevalence of Osteoarthritis of the Knee

OA of the lower leg may be present in people as early as 25 years. In 2001, a primary care trust population of 100,000 people in the southern parts of the United States of America, over the age of 55 years reported that: 25,000 people experienced knee pain for at least one month out of the year; 4,000 people that consulted a doctor for knee pain were diagnosed with OA; and 15,000 people suffered from a severe and debilitating form of OA of the knee (Peat et al., 2001).

A comprehensive clinical assessment looked at a sample of males and females, over the age of 45 years in South Africa. The assessment used the Kellgren & Lawrence criteria for the severity of osteoarthritis, proving the prevalence of OA of the knee. The above-mentioned assessment showed that African women of the Tswana population of Phokeng, South Africa, were at a greater risk of developing symptomatic OA of the knee than men. In addition, data showed that African American women were at a greater risk of developing OA of the knee than Caucasian women, whom were more prone to development of OA of the hip, along with European Caucasians, Jamaican and African blacks, and the Chinese (Woolf and Pfleger, 2003).
The prevalence of OA of the knee in adults living in the United States of America (USA) has
grown from a reported 21 million in 1990, to a total estimate of 26.9 million in 2005 (CDC,
2011). A 2008 U.S. population-based study indicated that 50% of Americans from the southern
most states are at risk of developing symptomatic OA, in at least one knee, and that two in three
obese Americans are at risk of developing OA (Murphy et al., 2008).

In smaller developed European countries a total of 4.3 million adults, over the age of 50 years,
are affected by OA of the knee (Jordan et al., 2007). The prevalence of asymptomatic OA of the
knee, in adults over the age of 60 years, living in the United States was 37.4%. In this group, the
prevalence among the female population was greater than that of men, at 42.1% to 31.2%
respectively (Dillon et al., 2006.).

Approximately 10% of the world’s population over the age of 50 years have symptoms
associated with OA. The prevalence in developing countries is seen to be variable, with some
studies showing a lesser prevalence, while others have shown similar levels to those of
developed countries (Symmons et al., 2000).

It is said that 45% of women over the age of 65 years in developed countries have symptoms of
OA, with supportive radiological findings in 70% of them. A study published by the World
Health Organization in 2002, named (The Global Burden of Disease), showed that OA had
increased in prevalence from being the tenth leading cause of years lost to disability (YLD) at a
global level in 1990, to the fourth leading cause of YLD in 2000 (Symmons et al., 2000).

2.1.3 Risk Factors for Osteoarthritis of the Knee

There are various risk factors involved in the development of osteoarthritis of the knee. The most
common risk factors for the development of OA of the knee are as follows:

- Gender - up to the age of 45 years men are more frequently affected with OA of the knee
  than women. After age 45 this changes with the incidence in women out numbering the
  incidence in men;
- Age - the incidence of OA of the knee increases with age;
- Obesity - overweight or obese individuals have an increased risk of developing OA of the
  knee;
- Occupation and hobbies - sports injuries, occupational stress and repetitive trauma may
  contribute to the development of OA of the knee;
• Genetic predisposition - first generation relatives with OA of any joint may be a risk factor for development of OA of the knee;
• Congenital arthropathy - congenital disorders, such as hip dysplasia, may be a risk factor for development of OA;
• Trauma or injury - sports injuries or other trauma can lead to development of OA of the knee; and/or
• Previous diagnosis of inflammatory joint disease (Lau et al., 2000; Murphy et al., 2008; Davis, 2013).

2.2 Anatomy and Physiological Function of the Knee

The knee joint is composed of osteological articulations between bones. Movements and range of motion are facilitated through an intricate network of cartilaginous components, including articular cartilage, meniscal cartilage, synovium and synovial fluid of the joint. Additional structures integral to the joints’ functionality include the bursae of the knee joint, the capsular ligaments, muscular components, blood supply and nerves (Davis, 2013).

2.2.1 The Osteology of the Knee

The knee is a uni-axial hinge joint composed of three main osteological structures: the femur, the tibia and the patella. The knee is a tri-compartmental, synovial condylar joint consisting of medial and lateral tibiofemoral compartments and the patellofemoral compartment. The tibiofibular articulation of the knee joint is the least impactful osteological component of the joint, and is constructed via articulations of the lateral condyle of the tibia and the head of the fibula (Sinnatamby, 2011).
Figure 2.1 Anterior View of the Osteology of the Knee Joint (Abrahams et al., 2003).

The femur is the largest long bone in the body, with a slightly asymmetrical distal end. The distal end of the femur provides numerous attachments for tendons and ligaments of the knee joint. The medial epicondyle has a convex eminence where the medial collateral ligament (MCL) attaches to the femur. The lateral epicondyle serves as an attachment site for the femoral portion of the lateral collateral ligament (LCL) (Tria and Scuderi, 2010).

The tibia is a smaller long bone than the femur. The proximal part of the tibia articulates with the distal femur via the medial and lateral epicondyles. The central portion of tibia, between the two condyles, exhibits an intercondylar eminence with an intercondylar notch. This portion serves as an attachment site for the anterior horn of the lateral meniscus and the anterior cruciate ligament (ACL). Anteriorly, a tubercle provides attachment for the patellar tendon, while anterolaterally, Gerdy’s tubercle serves as an attachment site for the illiotibial band (ITB) (Tria and Scuderi, 2010).

The patella is a sesamoid bone whose anterior positioning provides protection for the knee, as part of the joint’s extensor mechanism (Martini, 2006). The posterior portion of the patella articulates with the patellar surface of the trochlea of the femur. The stability of the patella is variable and may be based on morphological variations (Tria and Scuderi, 2010).
2.2.2 Cartilaginous Structures of the Knee

The cartilaginous structures of the knee can be divided into two main categories: articular cartilage and meniscal cartilage. The articular cartilage and meniscal cartilage of the knee joint reside adjacent to one another, and although completely different in structure, they exhibit a synergistic functionality exclusive to diarthroidal joints such as the knee (Flandry and Hommel, 2011).

Figure 2.2 Anterior, Posterior, Superior and Coronal Views of the Cartilage of the Right Knee (Moore and Dalley, 2006).

2.2.2.1 Articular Cartilage

Articular cartilage, also known as hyaline cartilage, may be distinguished from meniscal cartilage by its structure, elasticity, and tensile strength (Romanelli et al., 2008). The structure and composition of the articular cartilage of the knee joint directly relates to its function, which includes lubrication of the osteological surfaces of the joints interfacing structures, to allow smooth and fluent motion, and facilitation of load transmission without friction. Articular cartilage has two main subdivisions that contribute to its mechanical behavior: a fluid
component, consisting of water and electrolytes, and a solid component, containing type II collagen, proteoglycans, glycoproteins and chondrocytes (Sophia-Fox et al., 2009).

Water is the most abundant of the major components of the joint articular cartilage. The cartilaginous components of the joint require considerable amounts of water for the purpose of lubrication. The osteological structures of the knee also require water for the lytic and blastic metabolic processes that facilitate the continual structural reconstitution of the bones (Poole et al., 2008). Cartilage does not receive nutrients by way of arterial supply; rather it is supplied with nutrients, in the form of electrolytes, by means of diffusion. Dehydrated joints devoid of water and electrolytes do not function optimally. This may be an additional cause or exacerbating factor in OA of the knee (Sarzi-Puttini et al., 2010).

Type II collagen contributes largely to the tensile strength of the cartilage, facilitating an interaction between the joints’ solid and fluid matrices while the joint is under the strain of compressive loading and range of motion, thereby preventing injury caused by hyperextension and abnormal rotation of the joint (Romanelli et al., 2008).

Proteoglycans are large biomolecules that consist of a protein core with glycosaminoglycan side chains. Compaction of the proteoglycans by weight bearing creates a moderate and normal degree of swelling pressure and movement of fluid under compression. This, in conjunction with normal collagen composition, provides the necessary “shock-absorption” mechanism integral for normal joint functionality (Huber et al., 2000).

The connective tissue matrix of the joint is largely comprised of glycoproteins, which facilitate adherence of various cellular components and other proteins to one another, thereby giving the joints connective tissue its tensile strength and pliant nature (Wittman, 2008). Glycoproteins have many functions, including the binding of vitamins, minerals, electrolytes, cations, and other substances, for various purposes within the joint. The specialized binding capacity of glycoproteins give the joint a unique absorptive ability, which allows for the absorption and assimilation of supplements such as glucosamine sulphate, found to improve the state of those suffering with OA of the knee (Holford and Brune, 2006).

Chondrocytic cells are specialized cells that are responsible for the production and maintenance of the extracellular matrix of joints’ cartilage, rendering them integral in the joints functionality (Muir, 1995; Huber et al., 2000).
2.2.2.2 Meniscal Cartilage

The menisci of the knee joint are two entirely separate, crescent-shaped structures that cover approximately two-thirds of each articulating surface of the proximal tibia. The peripheral edges of each of the menisci are thickened and convex, attaching to the inner most portion of the joint capsule. The internal aspect of each meniscus is thin and concave, exhibiting a free edge (Martini, 2006).

The menisci of the knee joint create a more intimate articulation between the proximal tibia and the distal femur in order to increase the contact area of bones, facilitating load transmission. They also improve the distribution of the synovial fluid within the joint, thereby preventing soft tissue impingement during motion (Tria and Scuderi, 2010).

The menisci of the knee are composed largely of type I collagen and, to a lesser extent, of non-collagenous proteins and type II and III collagen (Poole et al., 2001). In order to maximize functionality, the fibers are arranged circumferentially and radially, aiding in the absorption of compressive loads on the knee and providing functional rigidity (Davis, 2013).

2.2.3 The Joint Capsule of the Knee

The capsule of the knee joint envelops the entire synovial knee joint. It consists of two primary layers. The outer, more superficial layer, the *stratum fibrinosum* or fibrocartilage, is composed of avascular, achromatic, dense fibrous tissue. The inner layer, the *stratum synoviale*, or synovial membrane, is a secretory layer, which secretes synovial fluid (Snell, 2012).
2.2.3.1 Stratum Fibrinosum

The *stratum fibrinosum* or fibrocartilage provides attachment between the capsule and osteological structures of the knee joint. It consists of type II collagen, chondroitin and keratin sulphates. The ligamentous and tendonous components also contain high concentrations of chondroitin and glucosamine sulphate. Accumulation of large amounts of glycosaminoglycans and type II collagen increase pressure resistance in specific parts of the knee joint, especially in the medial and lateral parts of the joint. This causes areas of characteristic regional thickness in the joint capsule, which is dependent on the various stresses that the respective regions may endure. Various extracapsular ligaments, whose presence provide a measurable degree of stability and protect the joint from overloading, establish thickening of the joint capsule (Flandry and Hommel, 2011; Palastanga and Soames, 2012).

2.2.3.2 Stratum Synoviale

The *stratum synoviale* or synovial membrane is the innermost sheathing of the joint capsule of the knee, attaching to the periphery of the articular cartilage and lining the fibrocartilage outer layer. The expanse of the synovial membrane reaches both femoral and tibial condyles, the fibrocartilaginous discs of the tibial and femoral articulating surfaces, the posterior articulating
surface of the patella, and peripheries of the menisci (Chantra, 2012; Tagliafico and Martinoli, 2013).

2.2.3.3 The Synovial Fluid

Synovial fluid is a sterile, viscid, non-Newtonian fluid, identifiable by its whitish to pale yellow, yolk-like, gelatinous appearance (Fam et al., 2007). Synovial fluid is characteristically thixotropic, meaning its viscosity decreases, causing fluid thinning due to aging, periodic stress or trauma. The primary purpose of the synovial fluid of the knee joint is to reduce friction between the articular cartilages of the femur with the tibia, and the femur with the patella (Hui et al., 2012).

Synovial fluid contains various cellular components, including: Type A cells that produce and secrete the hyaluronic acid; Type B cells that secrete synovial fluid; and leukocytic and phagocytic cells (Hui et al., 2012). Changes in cellular composition may be observed in pathology or due to inflammatory processes, and therefore may be classified accordingly (Bhuanantanondh et al., 2012).

Synovial fluid contains large amounts of hyaluronic acid, secreted by the synovial cells. Hyaluronic acid is responsible for the increased viscosity of the synovial fluid. In addition, hyaluronic acid contributes to the elasticity of the joints articular cartilages and it provides lubrication between cartilage and the synovium. Synovial fluid also contains lubricin, a large water-soluble proteoglycan that is secreted by the fibroblastic cells of the synovial membrane and the chondrocytes of the articular cartilage (Blewis et al., 2007). Lubricin reduces friction between opposing articular surfaces and it is integral in facilitating the gliding action of tendons during the joints phases of movement, allowing for a fluency of motion (Kimberly et al., 2013).

2.2.4 The Bursae of the Knee

The bursae of the knee are fluid-filled pouches that surround the knee joint and, in some cases, communicate directly with the joint cavity. Bursae are representative of points of weakness of the knee joint and additionally enlarge the joint space. The bursae of the knee can be classified anatomically as anterior, lateral or medial (Moore and Dalley, 2006; Negahban et al., 2010).
The anterior bursae of the knee are:

- The suprapatellar bursa
- The prepatellar bursa;
- The deep infrapatellar bursa;
- The subcutaneous infrapatellar; and
- The pretibial bursa (Saunders, 2007; Chantra, 2012; Tagliafico and Martinoli, 2013).

The lateral bursae of the knee are:

- The lateral gastrocnemius bursa;
- The fibular bursa;
- The fibulopopliteal bursa; and
- The subpopliteal bursa (Saunders, 2007; Chantra, 2012; Tagliafico and Martinoli, 2013)

The medial bursae of the knee are:

- The medial gastrocnemius bursa;
- The anserine bursa; and
- The bursa semimembranosa (Levangie and Norkin, 2011; Chantra, 2012; Tagliafico and Martinoli, 2013)
2.2.5 Ligaments of the Knee

The ligaments of the knee joint are comprised of extra-capsular and intra-capsular ligaments. These ligaments function as a group of inter-related stabilizing and anchoring structures for bones of the joint (Moore, 2004).

![Diagram of the knee joint and ligaments](image)

**Figure 2.5 Ligaments of The Knee (Darling, 1999).**

2.2.5.1 Extra-capsular Ligaments of the Knee

There are five extra-capsular ligaments that arise as a continuation of the joints’ fibrous capsule (Bruyere et al., 2008). The extra-capsular ligaments of the knee are:

- The patellar ligament, which stabilizes and aligns the articulation of the patella and the femur;
- The fibular (or lateral) collateral ligament (FCL) or lateral collateral ligament;
- The tibial (or medial) collateral ligament (TCL);
- The oblique politeal ligament (OPL); and
• The arcuate popliteal ligament (Moore and Dalley, 2006; Tria and Scuderi, 2010).

2.2.5.2 Intra-capsular Ligaments of the Knee

The intra-capsular or cruciate ligaments of the knee joint are located within the joints’ capsule, but remain external to the synovial cavity (Moore, 2004). The functionality of these ligaments is established by their particular lattice-type orientation and attachment to the articulating osteological structures of the joint (Bruyere et al., 2008; Mullaji, 2008).

The intra-capsular ligaments of the knee are:

• The anterior cruciate ligament (ACL);
• The posterior cruciate ligament (PCL);
• The ligaments of Humphrey and the ligament of Wrisberg;
• The medial collateral ligament (MCL);
• The medial patellofemoral ligament;
• The posterior oblique ligament;
• The lateral collateral ligament (LCL); and
• The fabellofibular ligament (Moore and Dalley, 2006; Saunders, 2007; Bruyere et al., 2008; Mullaji, 2008; Standring, 2008; Levangie and Norkin, 2011)
2.2.6 The Musculature of the Knee

The musculature of the knee joint may be divided anatomically into anterior superficial muscles, posterior superficial muscles and deep accessory muscles. Mechanically, they may be divided into muscles that facilitate different types of motion, namely flexion, extension or rotation of the knee joint (Dinubile and Patrick, 2005).

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Main Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anterior Superficial Layer</strong></td>
<td></td>
</tr>
<tr>
<td>Quadraceps femoris:</td>
<td></td>
</tr>
<tr>
<td>Vastus intermedius, Vastus medialis, Vastus lateralis, Rectus femoris</td>
<td>Extend leg at knee joint</td>
</tr>
<tr>
<td><strong>Posterior Superficial Layer</strong></td>
<td></td>
</tr>
<tr>
<td>Sartorius</td>
<td>Flexion of the knee</td>
</tr>
<tr>
<td>Semimembranosus</td>
<td>Flexion and medial rotation of the leg while knee is flexed</td>
</tr>
<tr>
<td>Semitendonosus</td>
<td></td>
</tr>
<tr>
<td>Biceps femoris</td>
<td>Flexion and lateral rotation of the leg while knee is flexed</td>
</tr>
<tr>
<td><strong>Accessory Deep Layer</strong></td>
<td></td>
</tr>
<tr>
<td>Gastrocnemius</td>
<td>Plantar flexion of the ankle when the knee is extended.</td>
</tr>
<tr>
<td></td>
<td>Flexion of the knee</td>
</tr>
<tr>
<td>Popliteus</td>
<td>Rotation of the femur to unlock the knee</td>
</tr>
<tr>
<td></td>
<td>Weak flexion of the knee</td>
</tr>
<tr>
<td>Illiotibial Band with Tensor Fascia Latta</td>
<td>Support of the tibia and femur during standing Synergistic augmentation of flexion and extension when the knee is flexed or extended by respective muscles</td>
</tr>
</tbody>
</table>

Table 2.1 Musculature of the Knee Joint and their Related Actions (Moore and Dalley, 2006).
2.2.6.1 Movements and Range of Motion of the Knee Joint

The range of motion of a joint refers to the distance and the direction that a joint is able to achieve at its total potential. The various movements, and therefore range of motion, of the knee joint includes flexion, extension and rotation. Each specific normal range of motion is expressed in degrees, a description of angular measurement from axis of the knee joint. This may be seen in the table below (Loudon et al., 2010).

<table>
<thead>
<tr>
<th>Movement</th>
<th>Possible Degree</th>
<th>Muscles Facilitating Movements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extension</td>
<td>None</td>
<td>Qadriceps femoris</td>
</tr>
<tr>
<td>Flexion</td>
<td>120° with hip extension</td>
<td>Hamstrings; Gracillis;</td>
</tr>
<tr>
<td></td>
<td>140° with hip flexion</td>
<td>Sartorius; Gastrocnemius;</td>
</tr>
<tr>
<td></td>
<td>160° with passive motion</td>
<td>Popliteus</td>
</tr>
<tr>
<td>Medial Rotation</td>
<td>10° with flexion</td>
<td>With flexion:</td>
</tr>
<tr>
<td></td>
<td>5° with extension</td>
<td>Semimembranosus;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Semitendonosus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>With extension of non-weight bearing knee:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Popliteus</td>
</tr>
<tr>
<td>Lateral Rotation</td>
<td>30°</td>
<td>With flexion:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Biceps Femoris</td>
</tr>
</tbody>
</table>

Table 2.2 Movements of the Knee Joint (Loudon et al., 2010).

2.2.7 Arterial Supply and Venous Drainage of the Knee

The popliteal artery and its branches provide the blood supply of the knee. The popliteal artery is a continuation of the femoral artery, and begins as it passes through the adductor hiatus. At the border of the politeus muscle it terminates by dividing into the anterior and posterior tibial arteries (Mathews et al., 2010).
The five genicular branches of the popliteal artery, that provide arterial supply for the joint capsule and its ligaments, are the superior lateral artery, the superior medial artery, the middle, inferior lateral genicular artery and the inferior medial genicular artery, forming the genicular anastamosis of the politeal fossa, as can be seen in figure 2.6. The many and varied arteries that form the periarticular anastamosis of the knee provide a necessary collateral articulation for bypass of the popliteal artery in situations where the knee has maintained flexion for prolonged duration. Muscular branches of the popliteal artery supply the gastrocnemius, soleus and plantaris muscles (Mathews et al., 2010).

Venous drainage of the knee is provided by the popliteal vein that begins as a continuation of the posterior tibial vein, at the distal border of the popliteus muscle. The popliteal vein lies close to popliteal artery for the duration of its course. Superiorly, the popliteal vein receives supplementary drainage from the small saphenous vein within the popliteal fossa. Superiorly, the popliteal vein becomes the femoral vein (Moore, 2004).

2.2.8 The Nerve Supply of the Knee

Functionally, the nervous supply of the knee joint may be described as either motor, sensory or proprioceptive (Sharman et al., 2006). The motor nerves facilitate motion and gait, the sensory nerves facilitate awareness of sensations such as pain or temperature, and the proprioceptive
nerves facilitate awareness of spatial orientation and bodily position. For this discussion, anatomical division into anterior and a posterior supply will be used (Wheeless, 2011).

Posteriorly, the nervous supply of the knee is derived from the sciatic nerve, which is derived from the sacral plexus (L4, L5, S1, S2, S3). The sciatic nerve gives rise to one of the two main innervating structures of the knee, the tibial nerve. The obturator nerve, which arises from the lumbar spine (L2, L3, L4), provides the knee with additional nervous supply by innervating the popliteal fossa (Horner and Dellon, 2013).

![Figure 2.7 Nerves of the Knee (Gray, 1999).](image)

The tibial nerve is the larger of the sciatic nerves’ two main branching divisions and is responsible for innervation of the posterior musculature of the thigh, the posterior joint capsule and the synovium covering the cruciate ligaments. The main cutaneous supply of the posterior portion of the leg comes via the sural nerve, a branch of tibial nerve (Netter, 1997; Horner and Dellon, 2013).

The obturator nerve predominantly gives nervous supply to the medial posterior musculature of the thigh (Horner and Dellon, 2013).

Anteriorly, the main nervous supply of the knee in derived from 3 nerves: The femoral nerve, the common peroneal nerve and the saphenous nerve (Sharman et al., 2006).
The femoral nerve is the largest branch of the lumbar plexus, as can be seen in figure 2.7. It provides innervation to the fascia and a bulk portion of the anterior musculature of the thigh; additionally it provides cutaneous supply to the medial aspect of the thigh. The saphenous nerve provides nervous supply to the anteromedial joint capsule, the patellar tendon and the anteromedial cutaneous region. The common peroneal nerve and its branches provide innervation for the LCL, the inferior lateral capsule and the anterolateral portion of the knee joint, including the anterolateral cutaneous regions (Netter, 1997; O’Rahilly et al., 2008; Wheeless, 2011).

2.3 Pathophysiology and Clinical Implications of Osteoarthritis of the Knee

2.3.1 Pathophysiology of Osteoarthritis of the Knee

Chondrocytic cells are primarily responsible for initiation of the articular degeneration associated with OA of the knee. OA of the knee involves a cascade of inflammatory events and proliferative changes that lead to ongoing articular damage. Due to the varying articular stresses, whether acute or chronic, there is gross transmission of synovial inflammatory cytokines into the cartilage. This transmission leads to tissue damage on a macroscopic and microscopic level (Davis, 2011).

Chondrocytes are mechanical stress sensors that produce and secrete destructive proteolytic enzymes and inflammatory mediators in response to articular stresses. In an attempt to repair damaged tissue, chondrocytes increase the production of collagen and proteoglycans. Any form of heteromorphic stress of the joint manifests in an aggravated response by the chondrocytic cells of the joint. The above-mentioned results in degeneration and proliferation of abnormal compromised joint cartilage (Bronner and Farach-Carson, 2007).

The pathophysiological events of OA cause significant effects on the tensile properties of the joints articular cartilage. The initial evidentiary histological disruption within the individual collagen fibrils, progresses to a compromise in the integrity of all of the collagenous structures of the joint (Huber et al., 2000). Repair of the joints components occurs simultaneously, with the production of proteolytic enzymes. The influx of proteolytic enzymes causes further degradation of the joints’ cartilaginous structures. Inflammatory cytokines trigger additional inflammation, which fuels the cycle of chondrocyte production. Abnormal production of the joints functional
components results in the destruction of the synovium, leading to abnormal contact between the joints osteological structures (Kumar et al., 2007). The requisite tensile strength of the collagen fibres becomes lessened, and therefore a great deal of destructive oedematous swelling follows. An increase in the intracellular pressure gradient leads to a leakage of fluid out of the cartilaginous matrix. When the fluid is compressed out from the articular cartilage, drag forces between the fluid and the solid matrix begin to increase, leading to an increased rate of loading. The combination of inflammation, destruction and inflammation of the joint leads to the characteristic stiffness of the cartilage and joint, as well effusions characteristic of OA of the knee (Bronner and Farach-Carson, 2007).

Excessive proliferation of the joint components leads to joint enlargement and, irrespective of the primary injury site, eventual inclusion of all the tissues of the joint is an inevitable part of the pathophysiology of OA of the knee (Kumar et al., 2007). In addition to the destruction of cartilage, the bony portions of the joint become sclerosed and osteoporotic, leading to an increased incidence of fractures. The synovium becomes thickened in parts and devoid in others. The synovial fluid exhibits a decrease in elasticity and viscosity as a result of a decreased concentration of hyaluronic acid. The meniscal cartilage becomes worn down and/or infiltrated by defective joint fluid. The bone is in direct contact with bone, causing an audible or palpable crepitus, a common sign of OA of the knee. Muscle tendons undergo strain, as a result of friction, leading to tendonitis and contractures (Bronner and Farach-Carson, 2007). Muscle bulk and tone is lessened, capsule strength and ligamentous support decreases, and as a result, weight-bearing motion becomes more challenging and increasingly painful. Joint instability is a hallmark of OA of the knee, leading to a compensatory formation of osteophytes at the joint margins. Osteophyte formation occurs in an attempt to increase the stability of the joint (Kumar et al., 2007).

![Figure 2.8 Degenerative Joint Disease (Miyamoto et al., 2008).](image-url)
2.3.2 Signs and Symptoms of Osteoarthritis of the Knee

The most common symptoms of OA of the knee include:

- Pain that is ameliorated by rest and aggravated by weight bearing activities;
- Morning stiffness on waking that is ameliorated by movement that continues no longer than 30 minutes;
- Increasing difficulty with everyday movements and activities; and/or
- Joint inflammation (ACR, 2011).

As the disease progresses, there may be:

- Marked joint inflammation;
- Redness;
- Crepitation;
- Joint enlargement and deformities;
- Muscle weakness; and/or
- Joint instability (ACR, 2011).

The most severe cases of OA result in complete disability and an inability to walk (Porter and Kaplan, 2008).

2.3.3 Investigations for Osteoarthritis of the Knee

A diagnosis of OA of the knee can be made by a combination of clinical findings, laboratory tests and radiological findings. These diagnostic tools are used to differentiate OA from other similarly manifesting conditions (Porter and Kaplan, 2008).

2.3.3.1 Clinical Findings

A clinical diagnosis of OA is based on certain criteria: (i) morning stiffness lasting 30 minutes or less from waking; (ii) visible joint inflammation and redness; (iii) crepitation; (iv) osteological deformities; (v) muscle weakness; and/or (vi) joint instability (Punzi et al., 2005).

2.3.3.2 Radiological Findings

Some common radiological findings on an X-ray, MRI or CT scan include: (i) signs of a decrease in joint space due to degradation of bony and cartilaginous components; (ii) loss and abnormal reconstruction of cartilage; (iii) the presence of osteophytes; (iv) bone that may appear...
to be more or less dense, moth-eaten or degenerated in some areas; and/or v) oedematous effusions (Lozada, 2011).

2.3.3.3 Blood and Laboratory Testing

Blood and laboratory tests utilized for the diagnosis of OA may include a full and differential blood count (FBC), a comprehensive metabolic panel (CMP), urate levels, rheumatoid factor (RF), cyclic citrullinated peptide antibody (CCP), synovial fluid analysis, and two inflammatory markers: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (Bijlsma et al., 2011).

The following blood tests may be used to monitor the general health and wellbeing of patients, or monitor respective treatments. An FBC, is used to monitor the constituents of blood plasma, including red blood cells, white blood cells and platelets. A CMP consists of 14 tests that monitor the status of a person's organ function, and may be used to assess specific conditions, such as diabetes or kidney disease. A CCP antibody test (like RF) is best used to evaluate individuals whose clinical signs are suggestive of rheumatoid arthritis (RA) or those who have already been diagnosed with undifferentiated arthritis (Windgassen et al., 2011).

Rheumatoid factor (RF) is a laboratory test used to detect and measure rheumatoid factor in the blood plasma. An immunoglobulin M protein (IgM), RF, is produced by the immune system in a pathogenic state. As an autoantibody, RF, that attacks the system's own tissues rather than pathogenic or other foreign substances, leads to auto-immune inflammatory arthritis, known as rheumatoid arthritis (Shiel and Stoppler, 2008). Approximately 80% of patients with rheumatoid arthritis (RA) test positive for RF in their blood. Therefore, the RF test is a valuable tool for distinguishing between rheumatoid arthritis and osteoarthritis (AACC, 2013).

Synovial fluid analysis is a diagnostic special investigation used to determine the cause of joint pain and inflammation (Kalish, 2005). The test is conducted on a sample of the joints’ synovial fluid that is extracted from the joint with an extraction needle and syringe, a process known as arthrocentesis. Initial testing assesses the physical and chemical characteristics of the synovial fluid sample (Matsumo et al., 2008). Physical characteristics of the synovial fluid include appearance, viscosity, colour and degree of clarity. Chemical characteristics include the concentration of mucinous products, pH, and the presence or absence of solutes, electrolytes and protein. Microscopic evaluation is used to determine the presence or absence of adventitious
products such as white blood cells (WBC), red blood cells (RBC), urate crystals or pathogenic organisms (Bijlsma et al., 2011).

C-reactive protein (CRP) is an inflammatory marker that is not normally present in the circulatory system. CRP appears as a part of the inflammatory cascade in response to injury, infection, or the acute inflammatory process associated with conditions such as OA (Roberts et al., 2000). In addition to clinical findings, CRP is useful to diagnose arthritis. Additionally, it is used to monitor disease severity based on the degree of periodic inflammation, indicated by clinical findings. The normal accepted levels of CRP in blood are below 3 mg/L. CRP levels between 3 mg/L and 10 mg/L are an indication of the inflammatory process associated with OA. CRP levels, taken at one-month intervals for a period of four months, may prove to be diagnostically and therapeutically relevant in patients with the signs and symptoms of OA of the knee (Windgassen et al., 2011).

Erythrocyte sedimentation rate (ESR) is the rate at which erythrocytes sediment in the period of one hour. It is a haematological, non-specific measure of inflammation, due to the fact that it increases from any cause of inflammation such as OA of the knee (Bijlsma et al., 2011).

CRP and ESR may be used in conjunction to assess the treatment of chronic diseases associated with inflammation. Although ESR is a diagnostically and therapeutically reliable test to measure inflammation, it is recommended that CRP be used first and foremost for the purposes of diagnosing chronic inflammation. CRP may be used in conjunction with ESR to track its progression (Roberts et al., 2000, Windgassen et al., 2011).

Blood and laboratory tests utilized to establish a conclusive diagnosis of OA include: RF to differentiate OA from RA, CRP to assess high levels of inflammation, urate levels to exclude gouty arthritis as a diagnosis, and synovial fluid analysis as explained above (Bijlsma et al., 2011).

2.3.4 Assessment Tools for Osteoarthritis

2.3.4.1 Arthritis Impact Measurement Scales (AIMS/AIMS2-SF)

Arthritis Impact Measurement Scales (AIMS/AIMS2-SF) are disease-specific measurement tools developed by Robert F. Meenan, The Dean of Boston University School of Public Health (Ren et
AIMS are utilized to assess the physical, social and emotional well being of those suffering with chronic disease. The AIMS2-SF is a short form of the AIMS2, designed as a measure of outcome in arthritis with nine scales that include: mobility, leg functionality (walking, bending, lifting), physical activity, household activity (managing money, medications and housekeeping), social activities, activities of daily living, pain and mental affection (depression and anxiety). AIMS2-SF includes sections on social support and work ability. The questionnaire is self-administered, and relatively easy for patients to understand (Meenan et al., 2004).

2.3.4.2 Intermittent and Constant Osteoarthritis Pain questionnaire (ICOAP) and Short Physical Performance Battery (SPPB)

The Intermittent and Constant Osteoarthritis Pain (ICOAP) questionnaire was developed in order to measure the pain experienced by those suffering with the pain OA of the lower extremities. The scales’ application is most useful when trying to qualify the pain of those persons suffering with chronic and degenerative osteopathies. Constant pain is characterised as pain with an unremitting bruised and aching sensation. Intermittent pain is described as far more severe in intensity than constant pain, however it comes and goes. Distinguishing between the two types of pain has proven to be valuable in monitoring treatments of OA of the lower limb and the progression of its pathophysiology (Moreton et al., 2012).

The ICOAP consists of two subscales comprising 11 individual items. Five items deal with constant pain and six items deal with intermittent pain. The scale is utilized to qualify both the intensity of the pain experienced by the subjects, as well as the effect of pain on their quality of life. The items of the questionnaire use a five-point grading scale. 10 of the items of the ICOAP are worded in such a way to assess the intensity of pain, with the responses ranging from: 0 (not at all), 1 (mildly), 2 (moderately), 3 (severely) or 4 (extremely). Item seven deals with the frequency of the subjects’ pain and the responses may be either: 0 (never), 1 (rarely), 2 (sometimes), 3 (often) or 4 (very often). The ICOAP questionnaire is quite uncomplicated and may be administered by a tester or self-administered (Moreton et al., 2012).

The Short Physical Performance Battery (SPPB) is a test that is utilized in many types of research across the healthcare spectrum. It is used to measure the functionality of subjects’ lower extremities. Conduction of this assessment is simple, requiring minimal training for the tester (Freire et al., 2012).
The test consists of three areas of examination of function, using tasks that simulate daily activities. These areas are representative of tasks which are essential for the subjects’ independent living, making each component of the assessment an integral outcome measure for subjects with chronic and degenerative disease. The three areas of measure of the SPPB are: static balance, gait speed and sitting and rising from a seated position in a standard chair (Puthoff, 2010).

Static balance is an uncomplicated measure whereby the subject is asked to maintain up to three standing postures for a maximum of 10 seconds. If the subject is able maintain this posture for 10 seconds, he or she will perform a semi-tandem stance position held for 10 seconds, followed by a tandem stance posture, additionally held for up to 10 seconds (Puthoff, 2010).

The gait speed test is also an uncomplicated measure, taking approximately two minutes to complete. The subject is asked to walk at his or her normal pace for a total of four meters, while being timed with a stopwatch, from commencement to termination. This is repeated two times. The fastest time achieved is the time that is utilized as the recorded time (Richette et al., 2011).

Following the gait assessment the subject is required to stand from a seated position in a standard chair without the use of the upper extremities for assistance. Once the subject is able to complete one round of sitting, followed by rising, he or she is instructed to complete five rounds of sitting-standing as rapidly as is possible without any upper extremity assistance. The time taken to complete the five rounds of sitting-standing is recorded (Puthoff, 2010).

Careful analysis of numerous studies shows the SPPB to be a reliable tool, for use by healthcare professionals to monitor the past future and current states of wellness of their subjects and patients. The SPPB score has also shown to be useful in measuring improvement of patients following numerous interventions such as the use of medications or supplementation for the purpose of pain reduction in chronic and debilitating conditions such as OA of the knee (Freire et al., 2012).

This study made use of the AIMS-SFV2 and CRP levels, while the other part of the study, conducted by another researcher, tested the same sample using the SPPB and the ICOAP.
2.3.5 Complications of Osteoarthritis of the Knee

Chronic, long term OA of the knee may lead to complications that include:

- Bony cysts (Baker’s cysts);
- Bony overgrowth;
- Nerve root compression;
- Chronic pain and stiffness;
- Decreased range of motion; and/or
- Disability or an inability to function as prior to disease onset (ACR, 2011; Mayo Foundation for Medical Education and Research, 2011).

2.3.6 Types of Arthritis and Differential Diagnosis for Osteoarthritis of the Knee

2.3.6.1 Rheumatoid Arthritis

Rheumatoid arthritis (RA) is an auto-immune condition, where circulating systemic auto-antibodies attack the joints’ synovium. Inflammation of the joint space and damage of the cartilaginous structures and tissues leads to the debilitating signs and symptoms of the disease. RA is the most likely differential diagnosis of OA. RA causes joint stiffness and swelling, a dull and aching pain of the affected joints, debility and elevated CRP levels. RA differs in its presentation of OA in the following ways: It is more severe and acute in its onset; it usually presents in the small joints initially and in a bilateral fashion; and the digits express classical swan neck deformities with ulnar deviation of the hand. RA may also include extra-articular manifestations, including vasculitis, depression, severe fatigue, unexplained intermittent fevers and a positive RF (Jakobbson and Hallberg, 2002).

2.3.6.2 Psoriatic Arthritis

Psoriatic arthritis is an auto-immune condition characterized by inflammation of numerous joints and prevailing skin affections, in the form of psoriasis. The aetiology of psoriatic arthritis is unknown, however, it is associated with other auto-immune conditions and certain drug treatments. The condition most frequently affects men between the ages of 30 to 50 years old, and presents with swollen sausage-like fingers and toes, fatigue, unexplained intermittent fevers, morning stiffness for hours after rising, pitted nails and back pain (Ritchlin et al., 2009).
2.3.6.3 Infectious Arthritis
Infectious arthritis, also known as septic arthritis, is an acute arthropathy caused by a bacterial, viral or fungal infection of the joint. It is usually a complication of a traumatic injury or pre-diagnosed infective condition. Septic arthritis most often affects individuals who have undergone joint replacement surgeries. The condition is sudden in onset, and often necessitates treatment by antibiotic or antifungal medications. It presents with very high fever, skin rash, generalized myalgia and pain in the affected joints. CRP and ESR may also be elevated well above normal acceptable levels (Cade, 2011).

2.3.6.4 Gout
Gout is an acute, self-limiting, mono-arthropathy caused by the deposition of uric acid crystals into a specific joint, leading to sudden and intense joint pain. Concomitant signs and symptoms include rubor, increased temperature, swelling and tenderness of the affected joint. Gout predominantly affects joints in a unilateral fashion, usually affecting the great toe. Risk factors for gout resulting from increased deposition of uric acid levels include joint injury, obesity, excessive alcohol and red meat intake, hypertension, stress, drugs or kidney disease (Terkeltaub and Edwards, 2011).

2.3.6.5 Reiter’s Syndrome
Reiter’s syndrome is an inflammatory condition that develops following an infection of the intestinal or genito-urinary systems with Salmonella, Shigella, Campylobacter or Neisseria gonorrhoea. It is a reactive arthritis, characterized by inflammation of many joints and tendons. Reiter’s syndrome presents with arthropathy and one or more of the following conditions: cervicitis, cystitis, urethritis or prostatitis (Ritchlin et al., 2009).

2.3.6.6 Ankylosing Spondylitis
Ankylosing spondylitis is a chronic inflammatory condition of the spinal column leading to vertebral fusion and irreversible spinal rigidity. Early stage signs and symptoms of ankylosing spondylitis include lumbago and stiffness that continues for a minimum of three months. The aetiology of ankylosing spondylitis is unknown, however patients with this condition present with the genetic marker, HLA-B27 (Spier and Braun, 2011).

2.3.6.7 Bursitis and Tendonitis
Bursitis (inflammation of one or more bursae) and tendonitis (inflammation of a muscular tendon arising from strain or sprain of the affected tendon or associated muscle or muscle group)
are both characterized by localized pain, which is self-limiting, and usually results in a complete and uncomplicated recovery. Both bursitis and tendonitis are common differential diagnoses for OA (Reid et al., 2010).

2.4 Conventional Treatment of Osteoarthritis

Recommended conventional treatments for OA of the knee include various forms of prescription and over-the-counter medications, physiotherapy and surgery.

2.4.1 Medication

2.4.1.1 Analgesic and Anti-Inflammatory Medications

Pain management for arthritis is achieved by the use of the three main types of medications: Simple analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) and muscle relaxants (MIMS, 2010).

Simple analgesics, such as acetominophen (paracetamol), tramadol and codeine, are indicated for mild to moderate pain caused by OA of the knee (Shamoon and Hochberg, 2001). Some negative effects of common analgesic drugs include: Allergic reactions, dependency, liver and kidney damage, and sensitivity to non-steroidal anti-inflammatory drugs. As of 2009, the United States Food and Drug Administration issued a recommendation of no more than 650 mg of paracetamol to be used four to six hourly. (FDA, 2011). Anything above 650mg is considered to be excessive and could lead to toxicity (Woodcock, 2009).

NSAIDs, such as naproxen or ibuprofen, are used to reduce pain and aid in the reduction of inflammatory responses caused by arthritic conditions (Bradley et al., 2011). Some negative effects of common anti-inflammatory drugs include: Allergic reactions, dependency, liver and kidney damage, cardiovascular pathologies, blood disorders, gastric upset (intestinal bleeding, ulcers, nausea and constipation), neurological deficits (headache, drowsiness, dizziness, nervousness, visual disturbances, tinnitus, depression, fatigue, sedation and epilepsy) and additional sensitivity to other non-steroidal anti-inflammatory drugs (FDA, 2011). The American Geriatric Society (2007) has issued strong warnings against the prescription of NSAIDs and opiates for older OA patients for the above-mentioned reasons (Scott et al., 2000).
Robaxin and Robaxisal are common muscle relaxants used to help treat acute attacks of OA and other painful musculoskeletal conditions. Side effects of long-term use of muscle relaxants include gastrointestinal disturbances, blurred vision and vertigo, sedation, headache and fevers (MIMS, 2013).

Contra-indication for use of the above mentioned analgesics (excluding paracetamol), NSAID’s and muscle relaxants include pregnancy, lactation, psychiatric disorders and epilepsy (Shamoon and Hochberg, 2000).

2.4.1.2 Corticosteroid Medication
Corticosteroid therapy may also be used to relieve joint pain and chronic inflammation (Scott et al., 2000). Corticosteroid medication can be orally administered or injected into the affected joint however, injecting medications may lead to further destruction of the joint and its already sensitive components (MIMS, 2013). In addition, there is a strict limit to the allowance of cortisone used on OA patients due to the many known and unknown long term effects that include: Weight gain with dyslipidaemia, drug-induced hypertension, cataracts, insulin resistance or severe exacerbation of pre-existing diabetes mellitus, increased risk of infections, osteoporosis and resultant fractures (American Geriatric Society, 2007).

2.4.2 Physiotherapy
Physiotherapy is a rehabilitative therapy, used to assist patients in improving upon impaired physical abilities. Physiotherapy is an individualized modality, consisting of specified exercises and techniques used to treat people suffering with ailments such as OA of the knee. Therapeutic techniques include joint mobilization, hydrotherapy and massage. These therapies are all recommended to relieve muscle pain and spasm, increase range of motion, and prevent further degenerative disability (Carr et al., 2004).

2.4.3 Arthroplasty
Arthroplasty is a surgical knee replacement procedure. It is designed to reduce the symptoms of knee pathology, thereby improving the joints’ functionality. Arthroplasty may be implemented when other medical modalities no longer provide adequate relief from joint pain and/or disability resulting from OA of the knee. The degenerated, damaged components of the knee are replaced with artificial plastic and metallic components. Complications that may arise as a result of the arthroplasty include bleeding, infarction, pulmonary emboli and infection (Bruyere et al., 2008).
2.5 Supplementary and Dietary Advice for Osteoarthritis

2.5.1 Dietary Advice for Patients Suffering from Osteoarthritis

Research has shown that certain nutrients, found in a balanced diet, can decrease the signs and symptoms of OA of the knee by decreasing the amount of systemic inflammation within the body. Therefore, eating foods that are considered to be pro-inflammatory in nature would tend towards increasing the signs and symptoms of OA by increasing systemic inflammation. Therefore it is advisable for those suffering with inflammatory conditions such as OA, to consume more foods that are naturally anti-inflammatory as can be seen in the table below (Calder et al., 2011; Webb, 2011).

<table>
<thead>
<tr>
<th>Pro-Inflammatory</th>
<th>Dietary Constituents</th>
<th>Anti-Inflammatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bananas, peaches, citrus</td>
<td>Fruits</td>
<td>Cherries, berries, pears, prunes</td>
</tr>
<tr>
<td>Potatoes, tomatoes, eggplants</td>
<td>Vegetables</td>
<td>Cruciferous vegetables, asparagus, lettuce, dark leafy greens, carrot, pumpkin, sweet potatoes, squash</td>
</tr>
<tr>
<td>Wheat, oats, rye, corn</td>
<td>Grains</td>
<td>Brown rice, millet, sorgum, quinoa</td>
</tr>
<tr>
<td>Butter, fried food</td>
<td>Fats</td>
<td>Olive oil, avocado oil, flaxseed oil</td>
</tr>
<tr>
<td>Meat, dairy, eggs</td>
<td>Animal Products</td>
<td>Salmon</td>
</tr>
</tbody>
</table>

Table 2.4 Nutritional Guidelines for OA of the Knee (Holford and Burne, 2006).
2.5.2 Supplements Recommended for Osteoarthritis:

There are many supplements on the market that are considered to aid in the symptomatic relief of inflammatory conditions such as OA of the knee

- **SAMe**
  s-adenosylmethionine (SAMe) is a construct of the liver derived from methionine. SAMe may propagate chondrocytic cells and cartilage, and may decrease cytokine-induced chondrocytic lysis. SAMe is also used to treat depression, and is therefore integral in managing the depression that is often associated with chronic pain of OA (Webb, 2011).

- **Omega-3 oils**
  Essential fatty acids, such as omega 3 oils are predominantly derived from fatty fish. These oils promote decreased production and action of anti-inflammatory prostaglandins (Brien et al., 2008).

- **Devil's claw**
  Devil's claw (*Harpagophytum procumbens*) is an African indigenous plant. Devil's claw may be anti-inflammatory due to its effect on the inhibition of the cyclo-oxygenase-2 (COX-2) pathway. Devil's claw, taken alone or in combination with an NSAID, decreases the pain associated with OA of the knee (Chantra et al., 2000).

- **Turmeric**
  Turmeric (*Curcuma longa*) is a spice commonly used in Eastern cuisine. Curcumin, the pharmacologically active component of tumeric, is anti-inflammatory by nature, due to its inhibition of COX-2, prostaglandins and leukotrienes (Majid, 2012).

- **Ginger**
  Ginger (*Zingiber officinale*) is a well-known natural medicine used for arthritic and inflammatory conditions. Ginger exhibits anti-inflammatory effects by inhibition of the COX and lipoxygenase pathways, as well as possible effect on tumor necrosis factor (TNF) (Majid, 2012).

- **MSM**
  Methylsulfonylmethane (MSM) is a plant-based extract most commonly found in natural foliage, fruits and green vegetables. MSM exhibits anti-inflammatory and analgesic effects on animals, with preliminary research suggesting that it may decrease degeneration of joints (Wolfe, 2013).
2.6. OsteoEze Gold™, Glucosamine and Chondroitin, and Related Research on Osteoarthritis

2.6.1 OsteoEze Gold™

OsteoEze Gold™ is a dietary supplement that is currently available on the market. Each capsule contains glucosamine sulphate (500mg), chondroitin sulphate (281 mg), vitamin C (50mg) and manganese (1mg) (Venter, 2012).

As discussed in section 2.2, glucosamine and chondroitin are integral components of articular cartilage and the joint capsule. Used in combination, supplements containing glucosamine sulphate and chondroitin sulphate aim to treat the underlying cause of numerous joint pathologies, especially the degeneration of cartilage seen in OA of the knee (Long et al., 2001). Research has shown that a combination of 500mg glucosamine and 400mg chondroitin sulphate, three times daily, can provide support for osteoarthritic joints, thereby counteracting the symptoms of OA of the knee (Vidyasagar et al., 2004). The therapeutic dose for the glucosamine sulphate and chondroitin sulphate is 1500mg and 1200mg daily, respectively, for a minimum of three months. It has been suggested that the dosage may reduced thereafter to, 1000mg and 800mg of glucosamine and chondroitin respectively.

Glucosamine is an endogenous amino sugar required for the synthesis of glycoproteins and glycosaminoglycans. It is found in synovial fluid, ligaments, and other components of the synovial joint structures. Glucosamine exhibits anti-inflammatory effects on arthritic joints, and enable an increase in chondrocytic cellular metabolism (Gregory et al., 2008); (Matsumo et al., 2008). Exogenous glucosamine may be synthetically produced or derived from the exoskeletons of marine life. Because glucosamine is derived from shellfish, there is some concern that glucosamine may cause allergic type reactions in those who present with shellfish allergies (Brief et al., 2001). However, there have been no reported incidents from persons with shellfish allergies who take glucosamine as a nutraceutical joint supplementation. This may be due to the fact that the antigens are found within the meaty portions of shellfish and not the exoskeleton of the shell which are used as part of joint supplement formulations. The most commonly utilized forms of exogenous glucosamine are glucosamine hydrochloride and glucosamine sulfate (Gregory et al., 2008).
More than 20 randomized controlled trials world-wide have evaluated the use of glucosamine sulphate and its role in treating OA of the knee and hip. In 2005, a systematic review of trials evaluating the use of glucosamine sulphate in the treatment of OA identified that the pooled data from these trials showed that glucosamine sulphate significantly reduces the pain of OA of the knee and hip. It has been compared with analgesics and NSAID’s in the treatment of OA, showing that glucosamine sulphate is effective for reducing pain and improving joint function. The effect of glucosamine sulphate on joint-space narrowing suggests that it reduces knee joint–space narrowing resulting from OA with long-term treatment of three years or more (Gregory et al., 2008).

Chondroitin sulphate is an endogenous glycosaminoglycan. Glycosaminoglycans are foundational substances of the synovial joint matrix. Preliminary evidence has shown that long-term supplementation with chondroitin sulphate may slow the joint-space narrowing seen in the pathophysiology of OA. One meta-analysis showed that the use of chondroitin sulphate as a treatment for OA would be beneficial to those patients suffering with mild to moderate OA of the knee, seen to improve symptoms such as joint pain and stiffness. Early clinical trials, conducted before the year 2000, show that a combination of chondroitin sulphate and conventional analgesics more effectively reduces pain compared with treatment using analgesics alone. Chondroitin has proven safe for long-term supplementation, and is well tolerated among a wide range of patients (Gregory et al., 2008; Wandel et al., 2010).

Two clinical trials evaluating the specified combination of chondroitin, glucosamine and manganese show a marked reduction pain in patients with OA of the knee (Gregory et al., 2008).

The addition of vitamin C and manganese as anti-oxidants in the OsteoEze Gold™ formulation aids in collagen production and removal of free radicals from systemic tissues (Venter, 2012). These nutraceuticals have also been proven to show little drug withdrawal once use has ceased, and lack significant side effects and drug toxicity in association with their long-term use (Brief et al., 2001). The most recent findings stipulate that 5000 mg of vitamin C taken daily is the maximum dose that can be considered safe (Massey, 2005).
CHAPTER THREE

3. METHODOLOGY

3.1 Research Sample

Seventy seven participants, from a target group of males and females, between the age of 40 and 70 years, were recruited from print advertisements and by word-of-mouth (Appendix A) at the University of Johannesburg, Doornfontein campus (DFC). The study was approved by the Faculty of Health Sciences Higher Degrees and Ethics Committee.

3.2 Recruitment

Advertisements were placed at the Health Centre at the University of Johannesburg, DFC, and the Biokinetic clinic at the University of Johannesburg, Bunting Road campus.

3.3 Inclusion Criteria and Exclusion Criteria

3.3.1 Inclusion Criteria

Participants were included in the study if they:

- Were male or female between the ages of 40 and 70 years; and
- Presented with symptomatic OA of the knee, i.e. knee pain with at least two of the following five criteria: morning stiffness lasting less than 30 minutes, crepitus, bony tenderness, bony enlargement and no palpable warmth.

3.3.2 Exclusion Criteria:

Participants were excluded from the Study if they:

- Had any co-morbid conditions;
- Had any conditions with similar presentation to OA of the knee such as rheumatoid arthritis, gout, septic arthritis, injury and systemic lupus erythematosus (SLE);
- Had any shellfish allergy;
• Were currently using OsteoEze Gold™ and/or any other herbal or nutritional supplementation for OA of the knee in the month leading up to the start of the study;
• Regularly used or were dependent on non-steroidal anti-inflammatory medication (NSAIDs);
• Had a blood test showing a positive result for RF above 11m/mol; and/or
• Had a blood test showing ultra sensitive CRP level below 1mg/L.

Participants were advised to take paracetamol or aspirin instead of NSAIDs for duration of the study.

3.4 Research Design and Procedure

This was a 16-week, double-blind, placebo controlled study using matched pairs according to age, gender and severity of symptoms. This formed part of a group study that, using the same sample, tested the effects of OsteoEze Gold™ in the treatment of OA of the knee using the Intermittent and Constant Osteoarthritis Pain questionnaire (ICOAP) to assess quality and frequency of constant and intermittent knee pain, and the Short Physical Performance Battery (SPPB) to assess gait and functionality of the knee joint. The research was conducted at the University of Johannesburg, Doornfontein campus, Health Clinic. Prospective participants underwent a screening consultation (Appendix B) and were requested to sign a consent form to have blood taken to assess for rheumatoid factor (RF) and to establish a baseline CRP level (Appendix C). A nursing sister at the Health Clinic on DFC drew the blood and blood analysis was done by Contract Laboratory Service (CLS) and the National Health Laboratory Service (NHLS).

The participants satisfying both the inclusion and exclusion criteria were invited to partake in the study, and requested not to take any medication or supplements for OA of the knee for the duration of the study. Participants were allowed to take paracetamol for pain management, and the frequency and dosage was documented (Appendix D). Participants were advised not to take more than 650mg (two 325mg tablets) of paracetamol every four to six hours (FDA, 2011). The half-life of paracetamol (acetaminophen) is two to three hours for an adult. Therefore participants were also requested not to take any paracetamol on the days of consultation, as this may have interfered with the assessment results (McNeil Consumer Healthcare, 2012). In addition, participants were requested not to make any major diet or lifestyle changes during the study.
The participants were divided equally, using matched pairs according to age, gender and severity of symptoms, into a control and experimental group. Base-line levels of CRP were determined with an initial blood test. Quality of life was assessed with the AIMS2-SF lifestyle questionnaire (Appendix E) (Meenan et al., 2004) and vital signs were checked and recorded (Appendix F). The control group received a four-week supply of placebo capsules (126 capsules per bottle), while the experimental group received a four-week supply of the OsteoEze Gold™ capsules (126 capsule per bottle). The AIMS2-SF lifestyle questionnaire consists of nine scales that includes: mobility, leg functionality, physical activity, and social activities, activities of daily living, pain and mental and emotional state. Each of the nine scales derives an individual score ranging from ten to twenty five. All of the scales are added together in order to derive a cumulative total score. The AIMS2-SF was conducted at the initial, 8 week and final 16 week consultations. The results were compared to each other in order to assess the participant’s progress (Meenan et al., 2004).

The participants had blood drawn from them by a qualified nursing sister at the initial consultation, the eight-week consultation and at the final 16-week consultation. This was for the purpose of assessing the inflammatory marker C-reactive protein (CRP). Assessment of the initial CRP levels allowed the researchers to establish a baseline reading, indicative of the participant’s levels of inflammation, resulting from OA of the knee. The follow-up blood analyses would therefore allow monitoring of the levels of inflammation over the course of the trial. Each of the participants received a Participant Medication Record used to record: (i) how many capsules of OsteoEze Gold™ placebo were taken each day; (ii) if any side-effects were experienced; and (iii) if any analgesics were taken, the dosage taken and how many were taken (Appendix D). Placebo and medicated capsules, as well as Participant Medication Records, were issued at the initial and 8 week consultations. The Participant Medication Records were collected at the eight week and final 16 week consultations. The participant’s vital signs (blood pressure, respiratory rate, heart rate and temperature) were assessed at the initial, eight week and final 16 week consultations (Appendix F).

3.5 Medication Administration

Each OsteoEze Gold™ capsule contains 500mg glucosamine sulphate, 267mg chondroitin sulphate, 50mg vitamin C and 1mg manganese. The placebo capsules contained microcrystalline cellulose PH101 (520mg), talc USP 24 (20mg) and emyral white corn starch 100025 (60mg), but
looked identical to the OsteoEze Gold™ capsules (Venter, 2012). The placebo and medicated capsules were bottled and labelled in the same manner. The medication was produced and randomized by Nativa (Pty) Ltd in accordance with Good Manufacturing Practice as stipulated by the South African Medicines Control Council (MCC, 2003). One capsule was to be taken three times a day with meals. If one dose was missed, two capsules could be taken at the next dosage (Venter, 2012).

3.6 Reliability and Validity Measures

The medication and placebo capsules were manufactured by Nativa according to Good Manufacturing Practice (MCC, 2003).

The AIMS2-SF lifestyle questionnaire (Appendix E) has been used in many different countries around the world and by many different administrators. It has proved to be an effective tool in the assessment of the progression of osteoarthritis (Meenan et al., 2004).

The blood test for CRP is a valid way of assessing the undulating inflammation that occurs in those suffering with OA of the knee. It has been used effectively in numerous and various research trials, and is suitable for the age group as well as for the condition of OA (Windgassen et al., 2011).

The participants were requested to abstain from using any treatment for their OA except for paracetamol during the trial, and only when necessary. This approach has been utilized in recent research trials showing that paracetamol does not interfere with results (Vidyasagar, et al., 2004). Participants were advised not to take more than 650mg (two 325mg tablets) of paracetamol every four to six hours (FDA, 2011). The use of paracetamol itself was evaluated with the Participant Medication Record (Appendix D) to further assess the effectiveness of the treatment on pain during the 16-week period.

A professional nursing sister drew blood in privacy at the University of Johannesburg, Doornfontein Homoeopathic Health Clinic. Contract Laboratory Services, a registered laboratory transported the participant’s blood for analysis.
3.7 Data Collection

The objective data was obtained from the CRP blood test. The subjective data was obtained from the AIMS2-SF lifestyle questionnaire (Appendix E).

3.8 Statistical Analysis

The data was statistically analyzed with the assistance of a statistician at Statkon. Frequencies and descriptives were applied to the data. Crosstabs were used to analyze group and gender. A test for normality, the Shapiro-Wilk test, was applied. The subsequent tests were used to draw a comparison between groups (inter-group). If the Shapiro-Wilk test result was normal, then this was be done with a t-test, and if the result was abnormal, the Mann-Whitney test was to be utilized. Next, comparisons within groups over time (intra-group) were carried out. This was done using the Friedman test. If differences over time within the groups were found, a Wilcoxon signed ranks test was applied to find out where these differences occurred (Becker, 2011).

3.9 Ethics

Participation in this research was completely voluntary and participants were able to leave the study at any point. The eligible participants signed a Participant Information and Consent Form (Appendix B) before starting the study which explained in detail all the procedures which would take place in the study. Participants were able to ask questions at any stage and these were appropriately answered by the researcher.

Participants were allowed to use paracetamol for pain relief. If the pain experienced by the participant became too severe, requiring the participant to use an alternative medication such as NSAIDs or corticosteroid therapy, the participant was excluded from the study and referred for further treatment.

There were no anticipated risks or side effects expected in taking OsteoEze Gold™ as any persons with shellfish allergy would have been excluded from the study. However, the participants were advised to discontinue the product immediately if any adverse reaction occurs (Venter, 2012). Confidentiality and anonymity was maintained, as identification details regarding participants are excluded from the dissertation and this information and case files are limited to researchers’ access only. Privacy was maintained as all consultations took place in a
private setting. The results of the study and which group participants were allocated to, was made available to every participant. Participants that were allocated to the placebo group had the opportunity to receive sixteen weeks of OsteoEze Gold™ from Nativa once the study has ceased. This research was approved by the ethics committee, the ethical clearance number is: AEC28-01-2012.
CHAPTER 4

RESULTS

4.1 Introduction

The aim of this study was to determine the effect of OsteoEze Gold™ on those participants suffering with symptomatic osteoarthritis (OA) of the knee. The objective data was obtained using biochemical analysis of the inflammatory marker C-reactive protein (CRP) over time. The subjective data was obtained using the Arthritic Impact Measurement Scales (AIMS2SF), to determine the participant’s relative qualities of life.

Seventy-seven participants were recruited into the study. Of the seventy-seven participants, 10 participants dropped out of the study, four of which were from the treatment group and six from the placebo group, stating that their pain had increased. A further nine participants dropped out of the study based on an inability to return to the clinic due to various personal difficulties. 48 participants completed the study.

4.2 Demographical Data: Gender and Age Distribution

There were a total of 27 participants in the treatment group. The mean age of the participants was 58.33 years, with a minimum of 43 years of age and a maximum age of 75 years of age. 24 participants were females, (55.8%), while there were 3 were males (60%).

There were a total of 21 participants in the placebo group, the mean age was 64.19 with a minimum age of 50 years and a maximum age of 74 years. 19 participants were female (44.2 %), while 2 were male (40%).

This shows that there were no significant variations in age or gender between the two groups.
4.3 Data Collection

4.3.1 Arthritis Impact Measurement Scale Short Form Version 2 (AIMS-SFV2)

The Arthritis Impact Measurement Scale (AIMS-SFV2) is a lifestyle-rating questionnaire consisting of 10 sections (identified as sections A-J) (Appendix E). The scales are predominantly used to determine the progression of each of the subjects perceived health and wellbeing. Subjects affected by chronic and degenerative disease, in both the placebo and treatment groups, were requested to answer a total of 45 questions concerning levels of mobility, self-care and household management abilities, social activity, emotional affect and over-all view of current and future health. The questionnaire was completed at the 1st consultation (week 0), the second consultation (week 8), and the final consultation (week 16). The 45 questions and their respective ratings are as follows:

Section A assessed the participant’s level of mobility during the past month by asking:

1. How often were you physically able to drive a car or use public transport;
2. How often were you able to be out of the house for at least part of the day;
3. How often were you able to run errands;
4. How often did someone have to assist you to get around outside of the house; and
5. How often were you in bed or a chair for most or all of the day?

Each question is rated from one to five as follows: All days (1); Most days (2); Some days (3); Few days (4); or No days (5).

A score of 13 would be the most desirable score one could achieve, denoting that ones’ mobility level was in fact optimal. A score of 17 would denote that ones’ mobility is greatly impaired to the extent of not being self-sufficient.

Section B assessed the participant’s ability to walk and bend during the past month by asking:

6. Did you have trouble doing vigorous activities;
7. Did you have trouble walking several blocks or climbing few flights of stairs;
8. Did you have trouble bending or stooping;
9. Did you have trouble walking one block or climbing one flight of stairs; and
10. Were you unable to walk unless assisted?
Each question is rated from one to five and rated as follows: All days (1); Most days (2); Some days (3); Few days (4); or No days (5).

A score of 21 is the most desirable score one could achieve, indicating that ones’ ability to participate in vigorous activities, walk and climb stairs was in fact optimal. A score of five would denote that ones’ ability to participate in vigorous activities, walk and climb stairs is greatly impaired, and therefore self-sufficiency is unmanageable.

Section C assessed the participant’s ability to perform self-care tasks during the past month by asking:

11. Did you need help to take a shower;
12. Did you need help to get dressed;
13. Did you need help to use the toilet; and
14. Did you need help to get in or out of bed?

Each question is rated from one to five and rated as follows: Always (1); Very often (2); Sometimes (3); Most always (4); or Never (5).

A score of 20 would be the most desirable score, showing that ones’ ability to care for ones’ personal needs was in fact optimal. A score of four would denote that ones’ ability to care for ones’ personal needs is greatly impaired, making self-sufficiency unmanageable.

Section D assessed the participant’s ability to complete household tasks during the past month by asking:

15. If you had the necessary transportation, could you shop for groceries without help;
16. If you had household tools, could you prepare your own meal without help;
17. If you had household tools and appliances, could you do your own housework without help; and
18. If you had laundry facilities could you do your own laundry without help?

Each question is rated from one to five as follows: Always (1); Very often (2); Sometimes (3); Most always (4); or Never (5).

A score of four would be the most desirable score one could achieve, as it would show an increased ability to undertake and complete household tasks. A score of 20 would denote that
ones’ ability to undertake and complete household tasks is greatly impaired, making self-sufficiency unmanageable.

Section E assessed the participant’s social activity over the past month by asking:

19. How often did you get together with friends or relatives;
20. How often did you have friends or relatives over to your home;
21. How often did you visit friends or relatives at their homes;
22. How often were you on the phone with friends or relatives; and
23. How often did you go to a church, club, meeting or other group?

Each question is rated from one to five as follows: All days (1); Most days (2); Some days (3); Few days (4); or No days (5).

A score of five would be the most desirable score one could achieve indicating an optimal level of ones’ social activity and desire to participate in social interactions. A score of 25 would denote that ones’ social activity and desire to participate in social interactions ability is greatly diminished and therefore might pose some cause for concern.

Section F assessed whether or not the participants received support from family and friends during the past month by asking:

24. Did you feel that your family and friends would be around if you needed their assistance;
25. Did you feel that your family and friends were sensitive to your personal needs;
26. Did you feel that your family and friends were interested in helping you solve your problems; and
27. Did you feel that your family and friends understand the affects of your arthritis?

Each question is rated from one to five as follows: Always (1); Very often (2); Sometimes (3); Most always (4); or Never (5).

A score of four would be the most desirable score, showing that one felt supported by family and friends. A score of 20 would denote that one did not experience support from family and friends, and therefore might pose some cause for concern.

Section G assessed the participants work activity during the past month by asking:

28. What has your main form of work been?
Each question is rated from one to five as follows: Paid work (1); House work (2); Unemployed (3); Disabled (4); or Retired (5).

If the answer to this question was either unemployed, disabled or retired, the following questions were omitted from the questioning procedure:

29. How often were you able to do any work (paid, school, house);
30. On the days that you did work, how often did you have to work a shorter day;
31. On the days that you did work, how often were you unable to work as carefully as you would have liked; and
32. On the days that you did work, how often did you have to change the way you do your work?

Each question is rated from one to five as follows: All days (1); Most days (2); Some days (3); Few days (4); or No days (5).

A preliminary score of three would give an indication that the subject does not engage in any form of formalized work, and would therefore not be subject to further questioning on the subject. A preliminary score of 1 or 2 would provide a basis for the remaining part of this section. A score of 20 would be the most desirable score one could achieve indicating that one’s ability to work, irrespective of the nature of the work was in fact optimal. A score of 4 would denote that one’s ability to work, irrespective of the nature of the work, is greatly diminished and therefore might pose some cause for concern.

Section H assessed participant’s levels of tension during the past month by asking:

33. How often have you felt tense or high strung;
34. How often have you been bothered by your nerves or nervousness;
35. How often have you been able to relax without difficulty;
36. How often have you felt relaxed or free of tension; and
37. How often have you have you felt calm and peaceful?

Each question is rated from one to five as follows: Always (1); Very often (2); Sometimes (3); Most always (4); or Never (5).

A score of 13 would be the most desirable score one could achieve, denoting that one felt relaxed and free of tension most or all of the time. A score of seventeen would denote that one
did not experience life in a relaxed manner, and was very stressed and therefore might pose some cause for concern.

Section I assessed the participants mood during the past month by asking:

38. How often have you enjoyed the things that you do;
39. How often have you been in low or very low spirits;
40. How often did you feel as though nothing turned out the way you wanted it to;
41. How often did you feel as though others would be better off if you were dead;
42. How often did you feel so low that nothing could cheer you up?

Each question is rated from one to five as follows: Always (1); Very often (2); Sometimes (3); Most always (4); or Never (5).

A score of 21 would be the most desirable score one could achieve denoting that one felt contented and enjoyed his/her day-to-day dealings. A score of nine would denote that one did not experience life in pleasurable way and therefore might pose some cause for concern.

Section J assessed the participant’s current and future state of health by asking:

43. How satisfied are you with your health right now;
44. How much of your health problem is due to your arthritis;
45. Considering all the ways your arthritis affects you, how well do you think you are doing compared to others your age?

Each question is rated from one to five as follows: Very satisfied (1); Somewhat satisfied (2); Neither satisfied nor dissatisfied (3); Dissatisfied (4); or Very dissatisfied (5).

A score of two would be the most desirable score one could achieve, showing that one felt he/she was in an advantageous state of health, whereby his arthritis is not a problem-causing factor in his life, and he/she is doing well compared to others in his/her similar disposition. A score of 15 would denote that one does not feel he is in state of wellbeing, his arthritis is the totality of his/her health problems and that comparatively he is suffering more than those in a similar disposition to himself/herself.
4.3.2 C-Reactive Protein

C-reactive protein is an inflammatory marker that is monitored by way of laboratory blood analysis (Roberts *et al.*, 2000). The normal accepted level of CRP in blood is below 3 mg/L. CRP levels between 3 mg/L and 10 mg/L are indicative of the inflammatory process associated with OA. CRP levels are diagnostically and therapeutically relevant in patients with the signs and symptoms of OA of the knee. (Windgassen *et al.*, 2011).

During this study, the participants’ CRP levels were assessed at the initial consultation (week 0), which served as the baseline reading, then again at the second consultation (week 8) and at the final consultation (week 16). The results were compared over time (Becker, 2013).

4.4 Inter-Group Analysis

4.4.1 Mann-Whitney

The Mann-Whitney statistical test is a nonparametric, inferential statistic that is utilized to determine whether two related samples show a statistically significant difference (Cohen *et al.*, 2011). In this study, the results from both the medication group and the placebo group were tested comparatively to determine whether there was a statistically significant improvement between the group receiving the medication and the group receiving the placebo for treatment of the signs and symptoms of osteoarthritis of the knee. The results compared were derived from the AIMS-SFV2 lifestyle questionnaire and the levels of inflammation as tested by the presence of blood plasma CRP.

A p-value < 0.05 suggests a statistically significant difference between the two groups in the two respective variables (Becker, 2013).
4.4.1.1 AIMS-SFV2 Inter-Group Analysis

At the commencement of the study (week 0) there were no statistically significant differences between the treatment and placebo groups in any of the AIMS-SFV2 components as none of the p-values were < 0.05 (Table 4.1). This would indicate that both groups were in similar standing at baseline.

<table>
<thead>
<tr>
<th>Week 0 AIMS Section</th>
<th>Group</th>
<th>Mean Rank</th>
<th>Z-value</th>
<th>Asymp. Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Placebo</td>
<td>22.71</td>
<td>-0.871</td>
<td>0.384</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>25.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Placebo</td>
<td>23.36</td>
<td>-0.502</td>
<td>0.616</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>25.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Placebo</td>
<td>25.90</td>
<td>-1.157</td>
<td>0.247</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>23.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Placebo</td>
<td>22.55</td>
<td>-1.122</td>
<td>0.262</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>26.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Placebo</td>
<td>24.26</td>
<td>-0.105</td>
<td>0.917</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Placebo</td>
<td>25.98</td>
<td>-0.691</td>
<td>0.490</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>23.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>Placebo</td>
<td>21.14</td>
<td>-1.491</td>
<td>0.136</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>27.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>Placebo</td>
<td>27.43</td>
<td>-1.292</td>
<td>0.196</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>22.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Placebo</td>
<td>24.95</td>
<td>-0.200</td>
<td>0.841</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J</td>
<td>Placebo</td>
<td>26.67</td>
<td>-0.954</td>
<td>0.340</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>22.81</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.1 Inter-Group Comparison with Mann-Whitney for Aims-SFV2 at Week 0
At the second consultation (week 8) there were no statistically significant differences between the treatment and placebo groups in any of the AIMS-SFV2 components with the exception of section F ($p = 0.040$), as shown in Table 4.2.

<table>
<thead>
<tr>
<th>Week 8</th>
<th>AIMS Section</th>
<th>Group</th>
<th>Mean Rank</th>
<th>Z-value</th>
<th>Asymp. Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Placebo</td>
<td>27.12</td>
<td>-1.391</td>
<td>0.164</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>22.46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Placebo</td>
<td>22.69</td>
<td>-0.794</td>
<td>0.427</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>25.91</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Placebo</td>
<td>24.38</td>
<td>-1.150</td>
<td>0.881</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24.59</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Placebo</td>
<td>25.02</td>
<td>-0.352</td>
<td>0.725</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Placebo</td>
<td>22.52</td>
<td>-0.865</td>
<td>0.387</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>26.04</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Placebo</td>
<td>28.71</td>
<td>-2.058</td>
<td>0.040</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>21.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>Placebo</td>
<td>20.93</td>
<td>-1.591</td>
<td>0.112</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>27.28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>Placebo</td>
<td>23.21</td>
<td>-0.567</td>
<td>0.571</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>25.50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Placebo</td>
<td>26.29</td>
<td>-0.807</td>
<td>0.419</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>23.11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>J</td>
<td>Placebo</td>
<td>27.33</td>
<td>-1.249</td>
<td>0.212</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>22.30</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.2 Inter-Group Comparison with Mann-Whitney for Aims-SFV2 at Week 8
At the final consultation (week 16) there were no statistically significant differences between the treatment and placebo groups in any of the AIMS-SFV2 (Table 4.3).

<table>
<thead>
<tr>
<th>AIMS Section</th>
<th>Group</th>
<th>Mean Rank</th>
<th>Z-value</th>
<th>Asymp. Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Placebo</td>
<td>25,14</td>
<td>-.318</td>
<td>.750</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24,00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>Placebo</td>
<td>22,29</td>
<td>-.972</td>
<td>.331</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>26,22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>Placebo</td>
<td>24,38</td>
<td>-.150</td>
<td>.881</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24,59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>Placebo</td>
<td>23,19</td>
<td>-.931</td>
<td>.352</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>25,52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E</td>
<td>Placebo</td>
<td>24,48</td>
<td>-.010</td>
<td>.992</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24,52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Placebo</td>
<td>27,12</td>
<td>-1,339</td>
<td>.181</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>22,46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>Placebo</td>
<td>21,12</td>
<td>-1,501</td>
<td>.133</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>27,13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>Placebo</td>
<td>24,71</td>
<td>-.094</td>
<td>.925</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24,33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Placebo</td>
<td>27,60</td>
<td>-1,388</td>
<td>.165</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>22,09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>J</td>
<td>Placebo</td>
<td>25,43</td>
<td>-.408</td>
<td>.684</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>23,78</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.3 Inter-Group Comparison with Mann-Whitney for Aims-SFV2 at Week 16

Statistical analysis did not show any statistically significant changes in any of the sections during the course of the study with the exception of section F as stated above. For section F, the optimal score was 4. At the first consultation (week 0) the mean was 6.952 and 6.519 for the placebo and treatment groups respectively. At the second consultation (week 8) the mean was 7.286 and 5.333 for the placebo and treatment groups respectively. These changes resulted in a statistically significant change (p = 0.030 and 0.040 with equal variances assumed).

4.4.1.2 C-Reactive Protein Inter-Group Analysis

C-reactive protein is an inflammatory marker that may be monitored by way of laboratory analysis (Roberts et al., 2000). The normal accepted level of CRP in the blood is below 3mg/L and 10mg/L is indicative of some inflammatory process associated with OA of the knee. CRP
levels are diagnostically and therapeutically relevant in patients with signs and symptoms of OA of the knee (Windgassen et al., 2011).

For this study, the CRP levels were assessed at the first consultation (0 weeks), the second consultation (8 weeks) and the final consultation (16 weeks).

Table 4.4 demonstrates that there was no statistically significant difference in the mean rank values for CRP over the course of the 16-week study (p > 0.05). This suggests that there was not a significant improvement in the abnormally elevated levels of CRP between the medication group and the placebo group.

<table>
<thead>
<tr>
<th>Week</th>
<th>Group</th>
<th>Mean Rank</th>
<th>Z-Value</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Placebo</td>
<td>25.57</td>
<td>-0.468</td>
<td>0.640</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>23.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Placebo</td>
<td>24.90</td>
<td>-0.177</td>
<td>0.860</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Placebo</td>
<td>24.60</td>
<td>-0.042</td>
<td>0.967</td>
</tr>
<tr>
<td></td>
<td>Treatment</td>
<td>24.43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4.4 Inter-Group Comparisons with Mann-Whitney for CRP-values at Week 0, Week 8, and Week 16.

4.5 Intra-Group Analysis

4.5.1 Friedman Test and Wilcoxon-Signed Ranks Test

The Friedman test is a non-parametric, statistical test, used to detect the presence of any differences in treatments across multiple test attempts. Known as a block design, whereby ranking of data by columns may establish the presence or absence of statistically significant changes. In this study, the point at which the data provided evidence for a statistically significant change within the two groups (p < 0.05) was then established by application of the Wilcoxon-Signed Ranks test (Mccluskey and Lalkhen, 2007).

The Wilcoxon Signed-Rank test is a non-parametric post-hoc statistical test of the works’ hypothesis, used in the comparison of repeated measurements on the same sample in order to assess whether their respective populations mean ranks differ, or two related samples, or matched samples. Here, the Friedman test detected significant statistical findings within the treatment group and therefore the Wilcoxon-Signed Ranks test determined at which point the treatment group showed a more positive response than the placebo group (Kuhnast and
4.5.2 AIMS-SFV2 Intra-Group Analysis

4.5.2.1 Section A: Mobility

Section A assessed the participant’s level of mobility during the past month. A score of 13 was the most desirable score one could achieve indicating an optimal level of mobility. A score of 17 was indicative of greatly impaired mobility. The mean value obtained at the first consultation (week 0) was used as the baseline reading for each of the two groups. The mean values for the placebo and treatment groups at week 0 were 13.00 and 13.704 respectively.

At the second consultation (week 8), there was an increase in the mean value in the placebo to 13.524. From the second consultation (week 8) to the final consultation (week 16) there was a decrease in the mean value from 13.524 to 13.381, showing a slight decrease in the subject’s mobility level from week 0 to week 16.

At the second consultation (week 8), there was a decrease in the mean value in the treatment group to 12.593. From the second consultation (week 8), there was a subsequent increase in the mean value from 12.593 to 13.222 at the final consultation (week 16) visit, showing a slight improvement in the subject’s mobility level from week 0 to week 16.
Figure 4.1 illustrates the mean values of the combined scores of the five questions of section A of the AIMS-SFV2.

Figure 4.1 The Mean Values for Section A of AIMS-SFV2

The Friedman test was used to determine the progression of the subjects’ levels of mobility as assessed by the AIMS-SFV2. The results of the Friedman test (Table 4.5) showed no statistical significance over time for the placebo group (p = 1.000) and treatment group (p = 0.097).

Table 4.5 Intra-Group Comparisons with Friedman Test for Section A of the AIMS-SFV2

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>0.000</td>
<td>4.667</td>
</tr>
<tr>
<td>Df</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>1.000</td>
<td>0.097</td>
</tr>
</tbody>
</table>

4.5.2.2 Section B: Walking and Bending

Section B assessed the participants’ walking and bending abilities during the past month. A score of 21 was the most desirable score one could achieve indicating an optimal ability to participate in vigorous activities, walking and climbing stairs. A score of five indicated that one’s ability to participate in vigorous activities, walk and climb stairs was greatly impaired.

At the first consultation (week 0), the mean value for the placebo group for section B was 14.429. This value was utilized as the base line reading. At the second consultation (week 8),
there was an increase in the mean value of the placebo group to 15.619. From the second visit (week 8) there was a further increase in the mean value from 15.619 to 15.762 at the final consultation (week 16), showing an overall improvement in the participants walking and bending abilities.

At the first consultation (week 0), the mean value for section B in the treatment group was 15.111. This value was utilized as the base line reading. At the second consultation (week 8), there was a noticeable increase in the mean value of the treatment group rising to 17.000. From the second visit at 8 weeks there was a subsequent increase in the mean value from 17.000 to 17.370 at the final consultation (week 16), showing an overall increase in the mean value of the treatment group of 2.259 and indicating an improvement in the participants’ ability to walk and bend.

Figure 4.2 illustrates the mean values of questions six through ten of section B of the AIMS-SFV2.

![Figure 4.2 The Mean Values for Section B of AIMS-SFV2](image)

The Friedman test was used to determine the progression of the subjects’ levels of mobility with specific reference to walking and bending as assessed by the AIMS-SFV2. Both groups showed an increase in the mean values from week 0 to week 16. The increase in the placebo group (1.333) was smaller than the treatment group (2.259). However, the Friedman Test showed no statistical significance, in either the placebo group (p = 0.336) or the treatment group (p = 0.128) over the course of the study.
4.5.2.3 Section C: Self-Care Tasks

Section C assessed the ability of participants to perform self-care tasks. A score of 20 was most desirable, indicating an optimal ability for one to care for one’s personal needs. A score of four was indicative that one’s ability to care for one’s personal needs was greatly impaired.

The mean value obtained at the first consultation (week 0) was used as the baseline reading for each of the two groups. The mean values for the placebo and treatment groups at week 0 were 19.857 and 19.481 respectively.

At the second consultation (week 8), there was an increase in the mean value of the placebo group, rising to 19.905. From the second visit (week 8) there was neither an increase nor a decrease; the mean value remained at 19.905 at the final consultation (week 16), showing a very slight improvement overall in the participants’ ability to perform self-care tasks from week 0 to week 16.

At the second consultation (week 8), there was an increase in the mean value of the placebo group, rising to 19.778. From the second consultation (week 8) there was a subsequent increase in the mean value from 19.778 to 19.815 at the final consultation (week 16), showing a slight improvement in the participants’ ability to perform self-care tasks.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>2.179</td>
<td>4.105</td>
</tr>
<tr>
<td>Df</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.336</td>
<td>0.128</td>
</tr>
</tbody>
</table>

Table 4.6 Intra-Group Comparisons with Friedman Test for Section B of the AIMS-SFV2
Figure 4.3 illustrates the mean values of questions 11 through 14 of section C of the AIMS-SFV2.

![Figure 4.3 The Mean Values for Section C of AIMS-SFV2](image.png)

The Friedman test was used to determine the progression of the subjects’ ability to perform daily requisite self-care tasks as assessed by the AIMS-SFV2. The Friedman test (Table 4.6) showed no statistical significance in section C of the AIMS-SFV2 over time in either the placebo group (p = 0.368) or treatment group (p = 0.174).

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>2.000</td>
<td>3.500</td>
</tr>
<tr>
<td>Df</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.368</td>
<td>0.174</td>
</tr>
</tbody>
</table>

Table 4.7 Intra-Group Comparisons with Friedman Test for Section C of the AIMS-SFV2

4.5.2.4 Section D: Household Tasks

Section D refers to the participants’ ability to complete household tasks during the past month. A score of four was the most desirable score, as it was indicative of an optimal ability to undertake and complete household tasks. A score of 20 was indicative of impairment in the ability to undertake and complete household tasks.
At the first consultation (week 0) the mean value for the placebo group for section D was 4.381. This value was utilized as the base line reading. At the second consultation (week 8), there was an increase in the mean value, rising to 4.905, indicating a slight decrease in the subjects’ ability to perform household tasks. From the second consultation (week 8) there was a decrease in the mean value from 4.905 to 4.429 at the final (week 16) consultation. Between week 0 and week 16 the mean value in the placebo group only changed by 0.048, showing that the participants ability to perform household task was not changed, even clinically.

At the first consultation (week 0), the mean value for the treatment group for section D was 5.481. This value was utilized as the base line reading. At the second consultation (week 8), there was a decrease in the mean value of the placebo group, lowering to 5.000. From the second visit (week 8) there was a subsequent increase in the mean value from 5.000 to 5.222 at the final consultation (week 16). This indicates a slight decrease in the participants’ ability to perform household tasks in the treatment group.

Figure 4.4 illustrates the mean values of questions 15 through 18 of section D of the AIMS-SFV2.

![Figure 4.4 The Mean Values for Section D of AIMS-SFV2](image)
The Friedman test (Table 4.8) was used to determine the progression of the subjects’ abilities’ to perform household tasks as assessed by the AIMS-SFV2.

The Friedman test showed no statistical significance in either the placebo or the treatment groups as their p-values were both \( p > 0.05 \) over time, as was assessed by the AIMS-SFV2 (placebo group \( p = 0.444 \) and treatment group \( p = 0.125 \)).

<table>
<thead>
<tr>
<th></th>
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<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>( N )</td>
<td>21</td>
<td>27</td>
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<tr>
<td>Chi-Square</td>
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<tr>
<td>( Df )</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.444</td>
<td>0.125</td>
</tr>
</tbody>
</table>

Table 4.8 Intra-Group Comparisons with Friedman Test for Section D of the AIMS-SFV

4.5.2.4 Section E: Social Activity

Section E refers to social activity over the past month. A score of five was the most desirable score one could achieve, indicating an optimal level of social activity, with a desire to participate in social interactions. A score of 25 indicated that one’s social activity and desire to participate in social interactions was greatly diminished and therefore might pose some cause for concern.

The mean value obtained at the first consultation (week 0) was used as the baseline reading for each of the two groups. The mean values for the placebo and treatment groups at week 0 were 12.667 and 13.111 respectively.

At the second consultation (week 8), there was a decrease in the mean value in the placebo group, lowering to 11.476. From the second consultation (week 8) there was a subsequent increase in the mean value from 11.476 to 11.762 at the final consultation (week 16), showing a slight improvement in the subjects’ social activities. However the Friedman Test (Table 4.9) showed that this change was not statistically significant \( (p = 0.744) \).

At the second consultation (week 8), there was noticeable decrease in the mean value, in the treatment group lowering to 12.667. From the second consultation (week 8) there was a subsequent decrease in the mean value lowering it from 12.667 to 11.593 at the final consultation (week 16), showing an overall improvement in the subjects’ social activity. The decrease in mean values from week 0 to week 8 was 0.444 with a further decrease of 0.074.
between week 8 and week 16. This resulted in a total decrease in the mean values for section E for the treatment group of 1.518. The Friedman Test (Table 4.8) showed this change to be significant with p < 0.05 (p = 0.019).

Figure 4.5 illustrates the mean values of questions 19 through 23 of section E of the AIMS-SFV2.

Due to the fact that the treatment group showed a statistical significance within section E of the AIMS-SFV2, the Wilcoxon-Signed Ranks test was applied to ascertain at which point during the study the significant changes occurred.

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
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<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>.593</td>
<td>7.918</td>
</tr>
<tr>
<td>Df</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.744</td>
<td>0.019</td>
</tr>
</tbody>
</table>

Table 4.9 Intra-Group Comparisons with Friedman Test for Section E of the AIMS-SFV
The Wilcoxon-Signed Ranks test showed that there was no statistically significant change between week 0 and week 8 (p = 0.657). The statistically significant change occurred between week 0 and week 16, with p = 0.012. This shows that there was a gradual improvement in the social activity of the treatment group over the course of the study.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th></th>
<th>Treatment</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Z</td>
<td>Asymp. Sig</td>
<td>Z</td>
<td>Asymp. Sig</td>
</tr>
<tr>
<td>Week 0 - 8</td>
<td>-.828</td>
<td>.408</td>
<td>-.445</td>
<td>.657</td>
</tr>
<tr>
<td>Week 0 - 16</td>
<td>-.592</td>
<td>.592</td>
<td>-2.516</td>
<td>.012</td>
</tr>
</tbody>
</table>

Table 4.10 Wilcoxon Signed Ranks Test for Section E of AIMS-SFV2

4.5.2.5 Section F: Support from Family and Friends

Section F refers to support from family and friends over the past month. A score of four was the most desirable score, indicating that the participant felt supported by family and friends. A score of 20 indicated that one did not experience support from family and friends, and therefore might pose some cause for concern. The mean value obtained at the first consultation (week 0) was used as the baseline readings for each of the two groups. The mean value for the placebo and treatment groups for section F was 6.952 and 6.519 respectively.

At the second consultation (week 8), there was a noticeable increase in the mean value in the placebo group, rising to 7.286. From the second consultation (week 8), there was a subsequent decrease in the mean value from 7.286 to 6.619 at the final consultation (week 16). This shows a slight improvement in the subjects’ sentiments pertaining to support from family and friends between week 0 and week 16.

At the second consultation (week 8), there was a decrease in the mean value in the treatment group, lowering to 5.333. From the second consultation (week 8), there was a subsequent further decrease in the mean value from 5.333 to 5.222 at the final consultation (week 16). This shows a larger improvement in the subjects’ sentiments pertaining to support from family and friends in the treatment group than the placebo group as mean values decreased by 1.297 and 0.333 respectively.
Figure 4.6 illustrates the mean values of questions 24 through 27 of section F of the AIMS-SFV2.

The Friedman test was used to determine the progression of the subjects’ sentiments pertaining to support from friend and family of the AIMS-SFV2. Although the mean values for the treatment group decreased more than in the placebo group, the Friedman Test (Table 4.9) showed that the change was not enough to be statistically significant. The p-values were $p = 0.232$ and $p = 0.294$ for the placebo and treatment groups respectively.

<table>
<thead>
<tr>
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<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>2.923</td>
<td>2.450</td>
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<tr>
<td>Df</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.232</td>
<td>.294</td>
</tr>
</tbody>
</table>

Table 4.11 Intra-Group Comparisons with Friedman Test for Section F of the AIMS-SF

4.5.2.6 Section G: Work During the Past Month

Section G refers to work during the past month. A preliminary score of three would indicate that the subject did not engage in any form of formalized work, and would therefore not be subject to further questioning within this section. A preliminary score of 1 or 2 would provide a basis for
questioning within this section. A score of 20 was the most desirable score one could achieve, indicating that ones’ ability to work, irrespective of the nature of the work, was optimal. A score of 4 would indicate that ones’ ability to work, irrespective of the nature of the work, is greatly diminished and therefore might pose some cause for concern.

At the first visit (week 0) the mean value for the placebo group for section G was 11.190. This value was utilized as the base line reading. At the second consultation (week 8) there was an increase in the mean value of the placebo group, rising to 12.048. From the second consultation (week 8) there was a further increase in the mean value from 12.048 to 12.810 at the final consultation (week 16), showing an overall improvement in the subjects’ ability to perform work tasks over the course of the study.

At the first visit (week 0) the mean value for the treatment group for section G was 13.778. This value was utilized as the base line reading. At the second consultation (week 8) there was an increase in the mean value, rising to 15.519. From the second consultation (week 8) there was a further increase in the mean value from 15.519 to 16.111 at the final consultation (week 16), showing an overall improvement in the subjects’ ability to perform work tasks over the course of the study.

The increase in the mean value was noticeably larger in the treatment group (2.333) than in the placebo group (1.620).

Figure 4.7 illustrates the mean values of questions 28 through 32 of section G of the AIMS-SFV2.
The Friedman test (Table 4.12) was used to determine the progression of the subjects’ ability to perform work tasks of the AIMS-SFV2. This test showed no statistical significance in the changes that occurred in either the placebo group (p = 0.444) or the treatment group (p = 0.294).

Table 4.12 Intra-Group Comparisons with Friedman Test for Section G of the AIMS-SFV

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Treatment</th>
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<tr>
<td>N</td>
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<tr>
<td>Chi-Square</td>
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<td>Df</td>
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<td>2</td>
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<tr>
<td>Asymp. Sig.</td>
<td>0.444</td>
<td>0.294</td>
</tr>
</tbody>
</table>

**Section H: Levels of Tension**

Section H refers to the levels of tension experienced by the subjects’ during the past month. A score of 13 was the most desirable score one could achieve, indicating that one felt relaxed and free of tension most or all of the time. A score of 17 was indicative that one did not experience life in a relaxed manner.

At the first consultation (week 0) the mean value for the placebo group for section H was 14.333. This value was utilized as the base line reading. At the second consultation (week 8) there was a decrease in the mean value, decreasing to 13.095. From the second consultation (week 8) there was a noticeable stabilization of the mean value from 13.095 to 13.095 at the final consultation.
(week 16), showing an overall decrease in the subjects' overall perception regarding levels of tension.

At the first consultation (week 0) the mean value for the treatment group for section H was 13.630. This value was utilized as the baseline reading. At the second consultation (week 8) there was an increase in the mean value, rising to 13.815. From the second consultation (week 8) there was a further increase in the mean value from 13.815 to 14.148 at the final consultation (week 16), showing a slight increase in the subjects' overall perceptions regarding levels of tension.

Figure 4.8 illustrates the mean values of questions 33 through 37 of section H of the AIMS-SFV2.

![Figure 4.8 The Mean Values for Section H of AIMS-SFV2](image)

The Friedman test (Table 4.11) was used to determine the progression of the subjects’ perceived levels of tension of the AIMS-SFV2. Although the mean value for the placebo group decreased by 1.238 and increased in the treatment group by 0.788, these changes were not statistically significant as the p-values were p = 0.296 and p = 0.987 respectively (Table 4.13).
### Table 4.13 Intra-Group Comparisons with Friedman Test for Section H of the AIMS-SFV

<table>
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<td>Df</td>
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<tr>
<td>Asymp. Sig.</td>
<td>0.296</td>
</tr>
</tbody>
</table>

#### 4.5.2.6 Section I: Mood

Section I refers to the subjects’ changes in mood during the past month. 21 was the most desirable score one could achieve indicating that one felt contented and enjoyed his/her day-to-day dealings. A score of nine indicated that one did not experience life in a pleasurable way. The mean value obtained at the first consultation (week 0) was used as a baseline reading for each of the two groups. The mean values for the placebo and treatment groups at the first consultation (week 0) were 18.333 and 17.815 respectively.

At the second consultation (week 8) there was a noticeable increase in the mean value in the placebo group, rising to 19.095. From the second consultation (week 8) there was an additional increase in the mean value from 19.095 to 19.333 at the final consultation (week 16), showing an overall improvement in the subjects’ perception regarding mood in the placebo group.

At the second consultation (week 8) there was an increase in the mean value in treatment group, rising to 18.704. From the second consultation (week 8) there was a subsequent decrease in the mean value from 18.704 to 18.603 at the final consultation (week 16), showing a slight improvement in the subjects’ perceptions regarding mood.

Figure 4.9 illustrates the mean values of questions 38 through 42 of section I of the AIMS-SFV2.
The Friedman test (Table 4.14) was used to determine the progression of the subjects’ mood of the AIMS-SFV2. The p-values for the treatment and placebo groups were 0.350 and 0.150 respectively, showing that the changes were not statistically significant.

<table>
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<td>Chi-Square</td>
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<td>Df</td>
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<td>2</td>
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<tr>
<td>Asymp. Sig.</td>
<td>0.150</td>
<td>0.350</td>
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</tbody>
</table>

Table 4.14 Intra-Group Comparisons with Friedman Test for Section I of the AIMS-SFV

Section J: Current and Future State of Health

Section J refers to the subjects’ current and future state of health. A score of two was the most desirable score one could achieve, indicating that one felt he/she was in an advantageous state of health, whereby his/her arthritis was not a problem-causing factor in his life, and he/she is doing well compared to others in his/her similar position. A score of 15 was indicative of the fact that one did not feel he/she was in a state of wellbeing, his arthritis is the totality of his/her health problems and that comparatively he/her is suffering more than those in a similar position to himself/herself.
At the first consultation (week 0) the mean value for the placebo group for section J was 9.048. This value was utilized as the base line reading. At the second consultation (week 8) there was a noticeable decrease in the mean value, decreasing to 7.714 from the second consultation (week 8) there was a further decrease in the mean value from 7.714 to 7.000 at the final consultation (week 16). This indicated an overall improvement in the subjects’ perceptions regarding their current and future health.

At the first consultation (week 0) the mean value for the treatment group for section J was 8.333. This value was utilized as the base line reading. At the second consultation (week 8) there was a noticeable decrease in the mean value, lowering it to 6.556. From the second consultation (week 8) the mean value remained unchanged at 6.556 at the final 16 week visit. There was however still an overall improvement in the subjects overall perceptions regarding current and future health from week 0 to week16.

Figure 4.10 illustrates the mean values of questions 38 through 42 of section J of the AIMS-SFV2.

![Figure 4.10 The Mean Values for Section J of AIMS-SFV2](image)

The Friedman test (Table 4.15) was used to determine the progression of the subjects’ perceptions of current and future health. The results thereof showed that changes in both groups were statistically significant for section J with p =0.005 in the placebo group and p = 0.026 in the treatment group.
In this study, the Wilcoxon-Signed Ranks test was utilized for section J because a statistically significant change was detected with the Friedman Test in both the placebo and treatment groups. Therefore the Wilcoxon-Signed Ranks test determined at which point the treatment group showed a more positive response to the treatment than the placebo group showed.

The mean value for the placebo group decreased by 1.334 from week 0 to week 8 and additionally decreased by 0.714 from week 8 to week 16. There was a total decrease in the mean value of 2.048 from week 0 to week 16. As these changes were sufficient to result in statistically significant changes for the placebo group in analysis with Friedman Test. The results of the Wilcoxon-Signed Ranks showed that the significant change did not occur between week 0 and week 8, where \( p = 0.059 \), but between week 0 and week 16 where \( p = 0.003 \).

The mean value for the treatment group decreased by 1.777 from week 0 to week 8, remaining unchanged at 6.555 from week 8 to week 16. Analysis by the Friedman Test \( (p = 0.026) \) lead to confirmatory analysis with the Wilcoxon-Signed Ranks Test, to show at which point in time the significant change occurred. The initial change that occurred between week 8 and week 0 was sufficient to result in two statistically significant values from the Wilcoxon-Signed Ranks Test for week 0 to week 8 \( (p = 0.012) \), as opposed to week 0 to week 16 \( (p = 0.031) \).

<table>
<thead>
<tr>
<th></th>
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<th>Treatment</th>
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<tbody>
<tr>
<td>N</td>
<td>21</td>
<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>10.528</td>
<td>7.324</td>
</tr>
<tr>
<td>Df</td>
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<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.005</td>
<td>0.026</td>
</tr>
</tbody>
</table>

**Table 4.15 Intra-Group Comparisons with Friedman Test for Section J of the AIMS-SFV**

In this study, the Wilcoxon-Signed Ranks test was utilized for section J because a statistically significant change was detected with the Friedman Test in both the placebo and treatment groups. Therefore the Wilcoxon-Signed Ranks test determined at which point the treatment group showed a more positive response to the treatment than the placebo group showed.

The mean value for the placebo group decreased by 1.334 from week 0 to week 8 and additionally decreased by 0.714 from week 8 to week 16. There was a total decrease in the mean value of 2.048 from week 0 to week 16. As these changes were sufficient to result in statistically significant changes for the placebo group in analysis with Friedman Test. The results of the Wilcoxon-Signed Ranks showed that the significant change did not occur between week 0 and week 8, where \( p = 0.059 \), but between week 0 and week 16 where \( p = 0.003 \).

The mean value for the treatment group decreased by 1.777 from week 0 to week 8, remaining unchanged at 6.555 from week 8 to week 16. Analysis by the Friedman Test \( (p = 0.026) \) lead to confirmatory analysis with the Wilcoxon-Signed Ranks Test, to show at which point in time the significant change occurred. The initial change that occurred between week 8 and week 0 was sufficient to result in two statistically significant values from the Wilcoxon-Signed Ranks Test for week 0 to week 8 \( (p = 0.012) \), as opposed to week 0 to week 16 \( (p = 0.031) \).

<table>
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<tr>
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<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Z</td>
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</tr>
<tr>
<td>Week 0 – 8</td>
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<td>0.059</td>
</tr>
<tr>
<td>Week 0 – 16</td>
<td>-2.935</td>
<td>0.003</td>
</tr>
</tbody>
</table>

**Table 4.16 Wilcoxon Signed Ranks Test for Section J of AIMS-SFV2**
4.5.3. C-Reactive Protein Intra-Group Analysis

The Friedman test was used to determine whether or not there was a statistically significant change in the CRP results of the sample, comparatively over-time. The data provided, consists of commencing the baseline value (week 0), following with the intermediate value (week 8) and terminating with the final value (week 16) as can be seen in Table 4.17 below, while the usefulness rank of the CRP values of the two sample groups over-time can be seen in Table 4.18.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>6.389</td>
<td>6.156</td>
</tr>
<tr>
<td>Week 8</td>
<td>6.905</td>
<td>6.712</td>
</tr>
<tr>
<td>Week 16</td>
<td>6.942</td>
<td>7.270</td>
</tr>
</tbody>
</table>

Table 4.17 Descriptive Statistics for CRP Over Time

In the placebo group the mean values changed from 6.389 at the first consultation (week 0) to 6.905 at the second consultation (week 8) to 6.942 at the final consultation (week 16). This shows a slight increase in the mean value from the first consultation through to the final consultation, showing no statistical significance (p = 0.334).

In the treatment group the mean values changed from 6.156 at the first consultation (week 0) to 6.712 at the second consultation (week 8) to 7.270 at the final consultation (week 16). This shows a slight increase in the mean value from the first consultation through to the final consultation, showing no statistical significance (p = 0.355)

<table>
<thead>
<tr>
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<th>Placebo</th>
<th>Treatment</th>
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</thead>
<tbody>
<tr>
<td>N</td>
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<td>27</td>
</tr>
<tr>
<td>Chi-Square</td>
<td>2.193</td>
<td>2.074</td>
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<tr>
<td>Df</td>
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<td>2</td>
</tr>
<tr>
<td>Asymp. Sig.</td>
<td>0.334</td>
<td>0.355</td>
</tr>
</tbody>
</table>

Table 4.18 Friedman Test Values for CRP Over Time
Using the Friedman test there was no noticeable statistical significance that was detected in the rankings of CRP over time for the placebo group ($p = 0.344$) or for the treatment group ($p = 0.355$).
CHAPTER 5

DISCUSSION

5.1 Introduction

This discussion chapter is an explanation of the results obtained from chapter four with the purpose of assisting in the understanding of the results of this research.

The inter-group analyses were conducted by means of the non-parametric Mann-Whitney statistical test. The Mann-Whitney test and the parametric t-test provided statistical evidence, showing differences between the distributions of the placebo group and the treatment groups available data. More specifically, they compared the distributions of the ranks of the scores at specified intervals within each group (Cohen et al., 2011).

The intra-group analyses were conducted by means of the non-parametric Friedman test and the Wilcoxon signed ranks test. These tests were conducted on the same variants in order to determine if any differences occurred during the course of the research and if so, at what precise stage of the study did they occurred. For the purpose of statistical analysis, final results are expressed in the form of a p-value. Any p-value <0.05, is considered to be a significant value, showing that there was a statistically significant change which is valuable to the research results. The Bonferroni adjustment was applied to the Wilcoxon signed-ranks test in order to reduce any chances of obtaining inflated or false-positive results. Once the Bonferroni adjustment has been applied, any statistically significant value would have to have been a p-value of <0.0125 (O'Donoghue, 2010).

The Friedman test and the Wilcoxon-signed Ranks test showed that both the medication group and the placebo group were not statistically significant in reducing moderate to severe baseline levels of C-reactive protein (CRP) in the blood tests and improving the quality of life (QOL) of those suffering with the signs and symptoms associated with osteoarthritis (OA) of the knee. According to the Friedman test, the medication group did perform better than the placebo group in two of the 10 sections of the AIMS-SFV2 questionnaire (Becker, 2013).

There was a significant improvement in section E, whereby subjects in the medication group expressed an increase in social activities, alluding to the fact that the sample was experiencing a
lessening in the severity of their symptoms as a result of taking the medication. The exact time frame where the improvement occurred was between the first visit at zero weeks and the third visit at 16 weeks, verified by the Wilcoxon-signed ranks test. Additionally there was a significant improvement in section J, whereby subjects in the medication group expressed a sentiment of betterment in their overall, current and future states of health (Becker, 2013). However there was also a statistically significant change in the placebo group for this section.

The Mann-Whitney test revealed that there was no significant difference between the mean rank values on any of the 10 AIMS-SFV2 subscales with the exception of section F at the second visit, at the 8-week interval as can be observed in Table 4.2. As can be observed in tables 4.1 and 4.3 there were no statistically significant differences in the mean rank values (p > 0.05).

Both groups obtained mainly statistically non-significant results for the Friedman test and the Wilcoxon-signed Ranks test. This shows that a diminished QOL, resulting from affection with OA of the knee, as tested with the AIMS-SFV2 was not seen to have a statistically significant improvement from supplementation with OsteoEze Gold™ with the exception of sections E and J. The Mann-Whitney test showed that OsteoEze Gold™ was not statistically significant in improving overall QOL and reducing above normal levels of CRP.

Even though the results showed statistical significance in two sections of the intra-group analysis and one section in the inter-group analysis, the null hypothesis can be rejected (Becker, 2013). When analysing the sections there were statistically significant improvements, the data suggests that the duration of the study was too short, as improvements only became significant between the initial consultation and the final consultation at 16 weeks.

5.2. Demographic Data

5.2.1. Age and Gender Distribution

Seventy-seven participants were recruited into the trial, and 48 completed the trial. The gender distribution revealed that the ratio between males and females was approximately 1:8.6. There were a total of 27 participants in the treatment group. 24 participants were females, while 3 were males. The mean age in the treatment group was 58.33 years. For the placebo group there was a total of 21 participants, 19 were female and 2 were male. The mean age was 64.19 years.
5.3 Inter-Group Analysis

The Mann-Whitney statistical test is a nonparametric inferential statistic that is utilized to determine whether two related samples show a statistically significant difference (Cohen et al., 2011). In this study the results from both the medication group and the placebo group were tested comparatively to determine whether there was a statistically significant improvement between the group receiving the medication and the group receiving the placebo for treatment of the signs and symptoms of osteoarthritis of the knee. The results compared were derived from the AIMS-SFV2 lifestyle questionnaire and the levels of inflammation as tested by the presence of blood plasma CRP. A p value < 0.05 suggests a statistical significance difference between the two groups in the two respective variables (Becker, 2013).

5.3.1 Inter-Group Analysis of AIMS-SFV2

As can be observed by Tables 4.1 and 4.3, the Mann-Whitney statistical test revealed that there were no significant differences between mean rank values on any of the 10 AIMS-SFV2 subscales, with the exception of Section F at time interval two, at 8 weeks (Table 4.2) (Becker, 2013).

Section F evaluated the support from family and friends during the past month and was scored as follows: Always (1); Very often (2); Sometimes (3); Most always (4); Never (5). A score of four would indicate that one felt supported by family and friends, while a score of 20 would denote that one did not experience support from family and friends and therefore might pose some cause for concern.

There is a definitive connection between people suffering with conditions of chronic pain and resultant mental and emotional conditions such as depression, chronic fatigue and anhedonism, accounting for the perceived states of loneliness, lack of familial and peer support and a general flat affect (Yohannes et al., 2010). Therefore it may be noted that once pain is even marginally alleviated, patients automatically experience a subsequent alleviation of their mental and emotional symptoms, seen within the treatment group of this trial.

A very plausible reason for this result having been statistically significant could be attributed and connected to the fact that participants in the treatment group were also experiencing an over all betterment of wellness as discussed in the intra-group analysis, with regard to the noticeable
statistical significance in section J, referring to over-all wellness currently and in the future, and section E, referring to an increase in participants’ social activities. The positive effects of the OsteoEze Gold™ was seen to have occurred during the duration of the trial between zero weeks and 16 weeks, with patients in the treatment group and in the placebo group, concluding an increase state of mental and emotional well-being with participants in both groups. It can therefore be concluded that supplementation with OsteoEze Gold™ could lead to a noticeable overall improvement in participants in the treatment group as opposed to those taking the placebo medication (Webb, 2011).

5.3.2 Inter-group Analysis of C-Reactive Protein

As can be observed in Table 4.4 there were no statistically significant difference in the mean rank values for CRP over the course of the 16-week study (p >0.05). The above mentioned suggests that there was not a significant improvement in the abnormally elevated levels of CRP between the medication group and the placebo group (Becker, 2013).

The suggested reason for the above-mentioned result could be based on a well-established correlation between obesity, cardiovascular disease (CVD) and OA of the knee, and the resultant elevation of blood plasma CRP (Richtte et al., 2011). Some of the afore mentioned conditions were apparent and/or concomitantly occurring in a great portion of the participants that took part sample in this study. While the inflammation associated with OA of the knee could have attributed to the high levels of CRP of the sample group, so too could it have been attributed to an underlying chronic CVD or the obesity itself, which was likely to have contributed to the severity of the OA of the knee (Richtte et al., 2011). Therefore, if the cause of the elevated blood plasma CRP was in fact obesity or CVD, and not primarily the OA of the knee, then it could be concluded that supplementation with OsteoEze Gold™ or other glucosamine sulphate and chondroitin sulphate based joint support products, may improve the suffering of OA the knee without, directly and positively showing an effect on elevated levels of blood plasma CRP (Matsuno et al., 2008).
5.4 Intra-Group Analysis

5.4.1 Intra-Group Analysis of the AIMS-SFV2

The quality of life of patients suffering from OA of the knee is significantly diminished (Dickson and Hosie, 2003). The AIMS-SFV2 assessed the impact that OA of the knee had on those participants on a monthly basis.

The Arthritis Impact Measurement Scale (AIMS-SFV2) is a lifestyle-rating questionnaire consisting of 10 sections is predominantly utilized to determine the progression of each of the subjects, perceived health and wellbeing. Subjects in both the placebo and treatment groups were requested to answer a total of forty-five questions concerning levels of mobility, self-care and household management abilities, social activity, emotional affect and over-all view of current and future health, commencing with week zero, following with the eighth week and terminating at the 16th week.

Section A assessed level of mobility during the past month. The results obtained from Section A of the AIMS-SFV2 showed, that according to the Friedman test, there was no statistically significant change in the treatment group (p = 0.097) or the placebo group (p = 1.000). The mean values did change from 13.000 to 13.381 in the placebo group and from 13.704 to 13.222 in the treatment group week 0 to week 16. This may show the possibility of an improvement in mobility, however a longer time period would be necessary.

Section B assessed the participants’ ability to walk and bend during the past month. The results obtained from Section B of the AIMS-SFV2 showed that, according to the Friedman test, there was no statistical significance in either the treatment group (p = 0.128) or the placebo group (p = 0.336). Analysis of the mean values additionally does not show significant clinical improvement, as reported in the participant scores for Section B.

Section C assessed self-care tasks during the past month. The results obtained from Section C of the AIMS-SFV2 showed that, according to the Friedman test, there was no statistical significance in the treatment group (p = 0.174) or the placebo group (p = 0.368). The mean values showed that there was an increase in the mean values of both the placebo (1.333) and treatment (2.259) groups from week 0 to week 16, with the change being greater in the treatment group than the placebo group.
Section D assessed the ability to complete household tasks during the past month. The results obtained from the Friedman Test on Section D of the AIMS-SFV2 showed that, there was no statistically significant change in the treatment group (p = 0.125) or the placebo group (0.444). Analysis of the mean values for both groups additionally showed that almost no change occurred in the clinical assessment by the participants.

Section E assessed social activity over the past month. The results obtained from Section E of the AIMS-SFV2 showed that, according to the Friedman test, there was a statistically significant change in the treatment group (p = 0.019), but not in the placebo group (p = 0.744). Results from the Wilcoxon Signed Ranks showed no statistically significant change between the first consultation at week 0 and the second consultation at week 8 (p= 0.657). When analyzing the trial period as a whole, week 0 through to week 16, one could conclude that the statistically significant change occurred between the second consultation (week 8) and the final consultation (week 16). The time interval at which the relevant change occurred leads to the understanding that a 16 week trial period was possibly too short to derive an accurate clinical result for a study of this nature. This could indicate that an improvement in the subjects’ quality of life (QOL) with regards to social activity, may be seen within 8 weeks or longer of treatment.

Section F assessed the participants’ perceptions pertaining to support from family and friends during the past month. The results obtained from Section F of the AIMS-SFV2 showed that according to the Friedman test, there was no statistical significance in the treatment group (p = 0.294) or the placebo group (p = 0.232). Analysis of the mean values from weeks 0 to 16, which relates closely to clinical improvement, did show a noticeably larger positive change in the treatment group (2.333) than in the placebo group (1.620).

Section G assessed the participants’ work type and quality thereof, during the past month. The results obtained from analysis with the Friedman Test of Section G of the AIMS-SFV2 showed that there was no statistical significance in the treatment group (p = 0.294) or the placebo group (p = 0.444). Analysis of the mean values from the first consultation at week 0 through to the final consultation at week 16, which relates to clinical improvement, did show a noticeably more positive change in the treatment group than the placebo group.

Section H assessed the levels of tension experienced by the participants during the past month. The results obtained from Section H of the AIMS-SFV2 showed that, according to the Friedman
test, there was no statistical significance in the treatment group (p = 0.987) or the placebo group (p = 0.296).

Section I assessed the participants’ mood during the past month. The results obtained from Section I of the AIMS-SFV2 showed, that according to the Friedman test, there was no statistical significance in the treatment group (p = 0.350) or the placebo group (p = 0.150).

Section J assessed the current and future state of health of each participant. The results obtained from Section J of the AIMS-SFV2 showed that, according to the Friedman test, there was a statistical significance in both the treatment group (p = 0.026) and in the placebo group (p = 0.005).

The Wilcoxon Signed Ranks Test was done to determine at which point in time the change had occurred. The test showed that the treatment group exhibited a statistically significant change between the first consultation at week 0 and the second consultation week 8 (p = 0.012) and from week 8 to the final consultation at week 16 (p = 0.031). In the placebo group the change was not significant from week 0 to week 16 (p =0.003) due to the application of the bonferoni adjustment. This could indicate that an improvement in the subjects QOL maybe seen within the first eight weeks of treatment. This shows that there was a clinical improvement in the participants’ (QOL) from 8 weeks into the trial period.

5.4.2 Intra-Group Analysis of C-Reative Protein

As can been seen in Table 4.22, the mean rank of CRP from the study’s’ commencement at week zero through to the studys termination at week 16, showed no statistical significance in the subjects CRP over time. This could be attributed to the fact that the elevated levels of CRP were not in fact caused by the inflammation of the osteoarthritis, but was due to some other unknown underlying causes (Richtte et al., 2011).

Therefore, though the OsteoEze Gold™ may have been effective in the improvement of general wellbeing, it did not have a positive effect on the lowering the elevated levels of CRP (Matsuno et al., 2008).
5.5 OsteoEze Gold™

OsteoEze Gold™ is a dietary supplement, clinically indicated for the treatment of OA of the knee (Vidyasagar et al., 2004). The following ingredients may be found in Nativa’s joint support formulation, OsteoEze Gold™, which was tested in this study.

Each capsule contains glucosamine sulphate (500mg); chondroitin sulphate (281 mg); vitamin C (50mg) and manganese (1mg) (Venter, 2012). In combination, such as with the OsteoEze Gold™ formulation, theses nutraceuticals aim to treat the underlying cause of numerous joint pathologies, especially the degeneration of cartilage as seen in OA of the knee (Long et al., 2001).

Glucosamine sulphate and chondroitin sulphate have also been proven to show little drug withdrawal once usage has ceased. Additionally, they lack significant side effects and drug toxicity in association with their long-term use (Brief et al., 2001).

OsteoEze Gold™ capsules were administered to 48 participants, three times daily for a total of 16 weeks, as a medicinal supplement, in order to prevent the degeneration of OA of the knee and aid in the reduction of the signs and symptoms of chronic degenerative arthropathy. This study was similar to a much larger scale study conducted by Vidyasagar et al., (2004) in India at the Kasturba Medical College, Manipal, Karnataka, India. In this study, the treatment group showed a significant improvement in the pain of OA of the knee when compared to the placebo group. In this study, the areas of the AIMS-SFV2 that showed improvement were predominantly seen in subjects’ sentiments regarding a general feeling of improved wellbeing, seen in sections E and J. Abnormally elevated levels of CRP did not show any significant improvement as a result of the 16 week of supplementation with OsteoEze Gold™.

In this study, OsteoEze Gold™ was administered three times a day for a total of 16 weeks. As was seen in the results chapter, there were no significant changes with regard to the levels of CRP between groups or within each group over time. In this study the only statistically significant changes were seen in sections E and J. Therefore a correlation may be seen with this 16-week study and the three-year study conducted by Vidyasagar et al., in 2004. This supports the hypothesis that long-term supplementation with joint formulations containing a combination of glucosamine sulphate and chondroitin sulphate could reduce the signs and symptoms of OA.
of the knee. A trend was observed that a general improvement in those affected with OA of the knee could be more profoundly evident the longer one supplements, as opposed to short-term supplementation (Matsuno et al., 2008). Improvement is not only limited to a physical improvement, but on an emotional and mental level as well.

5.6 The Placebo Effect

The placebo effect also known, as the placebo response is a phenomenon in which an undedicated or inactive substance is administered to an unknowing individual as medicine. The individual, thereafter experiences an improved state of health that may be solely attributed to the individuals’ expectation that the substance will result in wellness. It has been stated that the placebo effect is based only on a psychological response however; recent research indicates that placebos may also bring about a physical response, whereby patients actually show improvement in physical performance, as was seen in the placebo group of this study (Finniss et al., 2010).

There are two main theories of the placebo effect that exist within the area of medical research. The first in known as the subject-expectancy effect, where subjects have an understanding of the response the medication will elicit, said to have a subconscious effect on the subject, thereby causing the expected response. The classically conditioning effect is known as the expectation of relief resulting from taking a medication without prior knowledge of the medicines effect (Finniss et al., 2010).

Subject-expectancy and classical conditioning are similar, in that both effects, deal with the patients psychological expectation of the outcome. However the subject-expectancy effect is described as being ultimately subjective, due to the fact that any improvements are perceived and based strictly on the patients feedback, as was the case in this particular study. In section J participants within the placebo group showed a statistically significant improvement with regard to overall wellness between week 0 and week 16, which may be attributed to the subject-expectancy effect.

5.7 Limitations of the Study

- The sample size of this specific study was too small.
• The duration of the study was short. In similar trials with a longer duration results of the QOL questionnaires were more pronounced.

• The socio-economic standing of the large majority of the sample created a difficulty in compliance with respect to follow-up consultations. The sample complained that financing travel to appear for consultations was difficult and therefore accounted for a substantial number of dropouts.

• The language barrier between some of the members of the sample may have resulted in an inability of those to fully understand the questionnaire and therefore yielded inconclusive data with respect to any improvements or decrease of wellbeing.

• Patient compliance with regard to taking medication in the correct manner was a cause for concern in addition to patients taking non-steroidal anti-inflammatory medications for their pain.
CHAPTER 6

CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

This 16 week, pre-test post-test, double blind, placebo-controlled study documented the effect of OsteoEze Gold™ on the inflammatory marker C-reactive protein (CRP) and quality of life in OA of the knee using blood tests and the Arthritic Impact Measurement Scales (AIMS2SF), in men and women aged 40-75 years.

The intra-group analysis showed that the 48 participants whom were evaluated by means of the AIMS2SF, significant improvements in their perceived overall current and future health, support from friends and family and social abilities. Improvements occurred between weeks zero and eight weeks and continued from eight weeks to 16 weeks, indicating that the OsteoEze Gold™ joint supplement should be taken for a minimum of eight weeks in order to see its positive effects. The results additionally indicated that the OsteoEze Gold™ joint supplement did not prove effective in reducing abnormally high levels of CRP in those suffering with OA of the knee. OsteoEze Gold™ may be an effective treatment option for improving the quality of life of those suffering with OA of the knee. The inter-group analysis showed that the treatment group was no better than the placebo group and that the overall results in fact support the null hypothesis.

6.2 Recommendations

It would be recommended that:

- OsteoEze Gold™ be further tested by way of future studies and that those studies be conducted over a longer period of time, as it can be seen that the most significant results were seen to have occurred between zero weeks and 16 weeks of the study;

- Future studies testing the effect of OsteoEze Gold™ on osteoarthritis would use a larger sample group in order to be able produce relatively statistically viable results;
In any future studies the use of other medications including paracetamol and non-steroidal anti-inflammatory (NSAID’s) drugs by the sample be more closely monitored;

- Future studies may consider changing the research design, in order to test the effect of OsteoEze Gold™ in comparison to other complementary and alternative (CAM) treatments for OA of the knee rather than simply placebo; and/or

- In future studies that the researcher elicit the assistance of translators to conduct the lifestyle questionnaire for those participants whose primary language is not English. This would in turn lead to more accurate results in the area of the questionnaires.
REFERENCES


Kuhnast, C., Neuhauser, M. (2008). A Note on the Use of the Non-Parametric Wilcoxon-Mann-


Venter, A. (2012). Nativa Manufacturing – *OsteoEze GoldTM formulation*. Available at annemie@nativa.co.za or 012 664 6105.


Are you suffering with osteoarthritis of the knee?

Are you a male or female and between the ages of 50-70 years suffering from knee pain and stiffness when trying to perform your everyday activities?

We are conducting a research study for the Department of Homoeopathy at the University of Johannesburg, Doornfontein campus on:

The effect of OsteoEze Gold™ on inflammatory marker CRP and quality of life in osteoarthritis of the knee.

The effect of OsteoEze Gold™ on pain and functional ability in osteoarthritis of the knee.

This research study has been approved by the Faculty of Health Sciences Higher Degrees and Ethics Committee.

Ethical Clearance No:

If you are interested please contact:

ROMY: 072 107 6568 or KIM: 073 171 2060
APPENDIX B
CASE TAKING FORM – INITIAL CONSULTATION
C-Reactive Protein Level: _______________ Rheumatoid factor Level: _____________
Participant name: ______________________________ Assessment number: _______
Participant group: ______ Tester’s signature __________________________ Date: ______

PAST MEDICAL HISTORY:


FAMILY HISTORY:


CURRENT MEDICAL HISTORY:

Additional exams indicated:

Allergy to Shellfish:

Current use of NSAIDS or other pain medication:

Supplements:

Other medication:

SOCIAL HISTORY:


**PHYSICAL EXAMS:**

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<th>VITALS</th>
<th>Result</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>Respiratory rate</td>
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<tr>
<td>Pulse</td>
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<td>Temperature</td>
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<table>
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<tr>
<td>Palpation and active ROM</td>
<td></td>
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<tr>
<td>(including effusion tests)</td>
<td></td>
</tr>
<tr>
<td>Manoeuvres</td>
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</table>

**Diagnostic criteria for osteoarthritis of the knee:**

<table>
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<th>Knee pain and between ages of 50 years and 70 years with at least 2 out of the 5 following:</th>
<th>Tick if +</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crepitus</td>
<td></td>
</tr>
<tr>
<td>Morning stiffness less than 30 minutes</td>
<td></td>
</tr>
<tr>
<td>No palpable warmth</td>
<td></td>
</tr>
<tr>
<td>Bony enlargement</td>
<td></td>
</tr>
<tr>
<td>Bony tenderness</td>
<td></td>
</tr>
</tbody>
</table>

**Total score**

| 5 |

<table>
<thead>
<tr>
<th>OTHER EXAMS INDICATED</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
Any signs or symptoms of: | Tick if + | Comment |
---|---|---|
Rheumatoid arthritis |
Septic arthritis |
Acute gouty arthritis |
Systemic erythematous lupus |

Any further comments or observations:
APPENDIX C

PARTICIPANT INFORMATION AND CONSENT FORM

Dear prospective participant

Our names are Kim MacQuilkan and Romy Schneider. We are final year Homoeopathic students at the University of Johannesburg. We are inviting you to participate in this research study. We are undertaking this research study for our M Tech Homoeopathy qualification:

The effect of OsteoEze Gold™ on inflammatory marker CRP and quality of life in osteoarthritis of the knee
Romy Schneider
The effect of OsteoEze Gold™ on pain and functional ability in osteoarthritis of the knee
Kim MacQuilkan

Osteoarthritis (OA) is a common condition which affects the joints of the body. A person with OA often has pain, morning stiffness and decreased movement in the joint. OsteoEze Gold™ is an alternative treatment option for osteoarthritis which is currently available on the market. This product is considered to be safe for use, with no expected side effects. There is however a recommendation that shellfish allergy sufferers should not use this product. It contains glucosamine sulphate and chondroitin sulphate which are found in normal joints and aid in joint support. OsteoEze Gold™ also contains Vitamin C and manganese – these supplements are antioxidants which protect against the effects of aging on the joint.

We warmly invite you to participate in our research study if you have knee pain with at least or have three of the following:
- Over the age of 50 and 70 years
- Morning stiffness less than 30 minutes
- Crepitus (cracking of knee joint that you can hear and feel)
- Bony tenderness
- Bony enlargement

Please be aware of the following, which may exclude you from our research study.
If you have:
- Signs, symptoms or diagnosis of any chronic disease
• Conditions that may appear similar to OA of the knee such as rheumatoid arthritis (excluded with rheumatoid factor blood test), gout, septic arthritis or injury
• Suspected or known shellfish allergy
• Used or are using OsteoEze Gold™ or any other herbal or nutritional supplementation in the month leading to the start of the study
• Regularly used or are dependent on anti-inflammatory medication such as NSAIDS e.g. ibuprofen
• Blood test with positive result for rheumatoid factor (RF) over 1:40
• Level of an inflammatory marker called c-reactive protein (CRP) below 3mg/L

Our research aims to assess your symptoms of OA for a period of 16 weeks, consisting of an initial consultation, a follow-up consultation at 8 weeks and final assessment consultation at 16 weeks. Once you have signed this consent form and agreed to participate in this research study you will be requested to be present at the University of Johannesburg, Doornfontein campus, Homoeopathic Health Centre for consultations.

There are certain criteria that need to be evaluated before we can invite you to participate in this study. Two factors have to be assessed through a blood test: Rheumatoid Factor (a positive test will show that you have rheumatoid arthritis and not osteoarthritis) and C-reactive protein (CRP is a blood test that measures the inflammation in your body). This will be done by a qualified nursing sister at the University of Johannesburg Health Centre or Chris Hani Baragwanath Hospital. You may experience mild pain or discomfort while the nurse draws your blood for the test. Your blood samples will then be sent to Lancet Laboratory or National Health Laboratory Services for analysis.

You will be randomly allocated to one of two groups, either the experimental group or the placebo (control) group. This will ensure that the study is unbiased and the results will show if OsteoEze Gold™ proves more effective than the placebo. The experimental group will receive the OsteoEze Gold™ capsules. Each capsule of OsteoEze Gold™ 500mg glucosamine sulphate, 267mg chondroitin sulphate, 50mg vitamin C and 1mg manganese. The capsules will be given at initial consultation, four weeks, eight weeks and twelve weeks and will be labeled in such a way that neither you, nor we, will know who has received the treatment or who has received the unmedicated placebo. In addition you will receive a Participant Medication Record with which you are requested to record the number of capsules taken daily and any side-effects that may be experienced. You will be allowed to take paracetamol for severe pain- please record the amounts
taken accurately in the Participant Medication Record. These records will be collected every four weeks. Honesty with regard to record taking is very important to the results of the study. You will be requested not to take any paracetamol on the days that you have consultations as this may interfere with the results. If your knee pain becomes so severe that it requires you to take other forms of medication such as non-steroidal anti-inflammatories (NSAIDs) or corticosteroid therapy, you will be excluded from the study and referred for further treatment.

Each consultation (initial, eight week and sixteen week) will take place at the University of Johannesburg, Doornfontein Homoeopathic Health Clinic and consist of:

- Evaluation of your vital signs (blood pressure, heart rate, respiratory rate and temperature)
- Quality of life assessment known as the Arthritis Impact Measurement Scales (AIMS2SF)
- A pain questionnaire called the Intermittent and Constant Osteoarthritic Pain assessment
- A functional assessment known as the Short Physical Performance Battery
- Blood test tracking of the inflammatory marker CRP

The benefits of partaking in this study are regular check-up and the possible improvement of symptoms of OA of the knee through the use of a natural supplement, with less potential side-effects than conventional medication. The participation in this study is on a voluntary basis and you are free to withdraw from this study at anytime. A signed copy of this consent form will be made available to you. Individuals who were allocated to the placebo group, and did not receive the medicated capsules, will have the opportunity to be provided with sixteen week supply of OsteoEze Gold™, at no cost to you, once the research study has ended.

We have fully explained the procedure and the purpose of this study. We have also asked if the participant has any other questions relating to any part of this study and have answered and will be able to further answer any future questions to the best of our abilities.

Date: ______________________

Researcher: Kim MacQuilkan         Signature: ______________________

Researcher: Romy Schneider         Signature: ______________________
I have read this patient information and consent form. I have been fully informed about the procedures to be conducted in this research study. If at any time, I have more questions about this study, I understand that they will be answered by the researchers. In signing this consent form, I agree to fully undertake the tasks that are requested of me and understand that I may withdraw my participation at any time during the course of this study.

Date: __________________________

Participant: ______________________ Signature: __________________________

Supervisor: Dr Caminsky Signature: __________________________

CONTACT DETAILS:

Researcher: Kim MacQuilkan Supervisor: Dr. M. Caminsky
Cell No: 073 171 2060 Office No: 011 559 6701
Researcher: Romy Schneider Co-supervisor: Dr. G. Yutar
Cell No: 072 107 6568
APPENDIX D
PARTICIPANT MEDICATION RECORD

<table>
<thead>
<tr>
<th>Month</th>
<th>Number</th>
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<thead>
<tr>
<th>Name</th>
<th>Participant Group</th>
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Please make a note of how many capsules you have taken each day, any side effects you may have experienced and if and how many paracetamol tablets are taken each day for your osteoarthritic knee pain. Please include the dosage of paracetamol that you have taken (e.g. 1 x 500mg tablet).

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<thead>
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<th>Tuesday</th>
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<th>Saturday</th>
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<td>Side Effects</td>
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<td>Paracetamol</td>
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<td>2</td>
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</table>
APPENDIX E
ARTHРИTIS IMPACT MEASUREMENT SCALES 2 (AIMS2)

Month ________  Number ________
Name ______________________  Participant Group ________

Instructions: Please answer the following questions about your health. Most questions ask about your health during the past month. There are no right or wrong answers to the questions and most can be answered with a simple check (X). Please answer every question.

Please check (X) the most appropriate answer for each question.

**Section A: These questions refer to mobility level.**

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<th>Few Days</th>
<th>No Days</th>
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<td></td>
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</tr>
</tbody>
</table>

DURING THE PAST MONTH...

1. How often were you physically able to drive a car or use public transportation?

2. How often were you out of the house for at least part of the day?

3. How often were you able to do errands in the neighborhood?

4. How often did someone have to assist you to get around outside your home?

5. How often were you in a bed or chair for most or all of the day?

Total section A: ________/25

**Section B: These questions refer to walking and bending.**

<table>
<thead>
<tr>
<th>All Days</th>
<th>Most Days</th>
<th>Some Days</th>
<th>Few Days</th>
<th>No Days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


DURING THE PAST MONTH...

6. Did you have trouble doing vigorous activities such as running, lifting heavy objects, or participating in strenuous sports?

   (1)  (2)  (3)  (4)  (5)

   _____   _____   _____   _____   _____

7. Did you have trouble either walking several blocks or climbing a few flights of stairs?

   (1)  (2)  (3)  (4)  (5)

   _____   _____   _____   _____   _____

8. Did you have trouble bending, lifting or stooping?

   (1)  (2)  (3)  (4)  (5)

   _____   _____   _____   _____   _____

9. Did you have trouble either walking one block or climbing one flight of stairs?

   (1)  (2)  (3)  (4)  (5)

   _____   _____   _____   _____   _____

10. Were you unable to walk unless assisted by another person or by a cane, crutches, or walker?

    (1)  (2)  (3)  (4)  (5)

    _____   _____   _____   _____   _____

   Total section B: _____ /25

Section C: These questions refer to self-care tasks

DURING THE PAST MONTH...

<table>
<thead>
<tr>
<th>Question</th>
<th>Always (1)</th>
<th>Very Often (2)</th>
<th>Sometimes (3)</th>
<th>Almost Never (4)</th>
<th>Never (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. Did you need help to take a bath or shower?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Did you need help to get dressed?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Did you need help to use the toilet?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. Did you need help to get in or out of bed?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total section C: _____ /20

Section D: These questions refer to household tasks.
DURING THE PAST MONTH...

15. If you had the necessary transportation, could you go shopping for groceries without help?  

16. If you had kitchen facilities, could you prepare your own meals without help?  

17. If you had household tools and appliances, could you do your own housework without help?  

18. If you had laundry facilities, could you do your own laundry without help?  

Section E: These questions refer to SOCIAL ACTIVITY.

19. How often did you get together with friends or relatives?  

20. How often did you have friends or relatives over to your home?  

21. How often did you visit friends or relatives at their homes?  

22. How often were you on the telephone with close friends or relatives?
23. How often did you go to a meeting of a church, club, team or other group? _____ _____ _____ _____ _____

Total section E: _______/25

Section F: These questions refer to support from family and friends.

DURING THE PAST MONTH...

24. Did you feel that your family or friends would be around if you needed assistance? _____ _____ _____ _____ _____

25. Did you feel that your family or friends were sensitive to your personal needs? _____ _____ _____ _____ _____

26. Did you feel that your family or friends were interested in helping you solve problems? _____ _____ _____ _____ _____

27. Did you feel that your family or friends understood the effects of your arthritis? _____ _____ _____ _____ _____

Total section F: _______/20

Section G: These questions refer to work.

Retired
DURING THE PAST MONTH... (1) (2) (3) (4) (5)

Paid work
House work
Unemployed
Disabled
28. What has been your main form of work? _____ _____ _____ _____ _____

If you answered unemployed, disabled or retired, please skip the next four questions and go to the next page.

<table>
<thead>
<tr>
<th>Days</th>
<th>All</th>
<th>Most</th>
<th>Some</th>
<th>Few</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days</td>
<td>(1)</td>
<td>(2)</td>
<td>(3)</td>
<td>(4)</td>
<td>(5)</td>
</tr>
</tbody>
</table>

29. How often were you unable to do any paid work, housework or school work? _____ _____ _____ _____ _____

30. On the days that you did work, how often did you have to work a shorter day? _____ _____ _____ _____ _____

31. On the days that you did work, how often were you unable to do your work as carefully and accurately as you would like? _____ _____ _____ _____ _____

32. On the days that you did work, how often did you have to change the way your paid work, housework or school work is usually done? _____ _____ _____ _____ _____

Total section G: _______/25
Section H: These questions refer to level of tension.

DURING THE PAST MONTH...

<table>
<thead>
<tr>
<th>Very</th>
<th>Always</th>
<th>Often</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
</table>

(5)

33. How often have you felt tense or high strung?

____  ____  ____  ____

34. How often have you been bothered by nervousness or your nerves?

____  ____  ____  ____

35. How often were you able to relax without difficulty?

____  ____  ____  ____

36. How often have you felt relaxed and free of tension?

____  ____  ____  ____

37. How often have you felt calm and peaceful?

____  ____  ____  ____

Total section H: ______/20
Section I: These questions refer to mood.

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>Always</th>
<th>Often</th>
<th>Sometimes</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>38. How often have you enjoyed the things you do?</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>39. How often have you been in low or very low spirits?</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>40. How often did you feel that nothing turned out the way you wanted it to?</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>41. How often did you feel that others would be better off if you were dead?</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>42. How often did you feel so down in the dumps that nothing would cheer you up?</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
<td>_____</td>
</tr>
</tbody>
</table>

Total section I: _____/25
Section J: These questions refer to your current and future health.

Neither
Very Satisfied
Satisfied Somewhat Neither
 woven Dissatisfied
(1) (2) (3) (4) (5)

43. How satisfied are you
with your HEALTH NOW?

(0) (1) (2) (3) (4) (5)

44. How much of your problem
with your HEALTH NOW
is due to your arthritis?

(0) (1) (2) (3) (4) (5)

45. CONSIDERING ALL THE WAYS
THAT YOUR ARTHRITIS AFFECTS
YOU, how well are you doing compared
to other people your age?

(0) (1) (2) (3) (4) (5)

Total section J: /15
Section G: /25  
Section H: /20  
Section I: /25  
Section J: /15  

TOTAL: /220

APPENDIX F
CASE TAKING FORM – FOLLOW UP CONSULTATION
C-Reactive Protein Level: __________
Participant name: ___________________________ Assessment number: ______
Participant group: _______ Tester’s signature ______________________ Date: ______

PHYSICAL EXAMS:

<table>
<thead>
<tr>
<th>VITALS:</th>
<th>Result</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAJCOLD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Any further comments or observations: